

NEANDERTAL INTELLIGENCE  
Surprising Clues to What They Knew

ALZHEIMER'S ADVANCES  
New Keys to Thwarting Dementia

# SCIENTIFIC AMERICAN

June 2010

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Does  
**TIME**  
Really Exist?  
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Self-Aware Machines  
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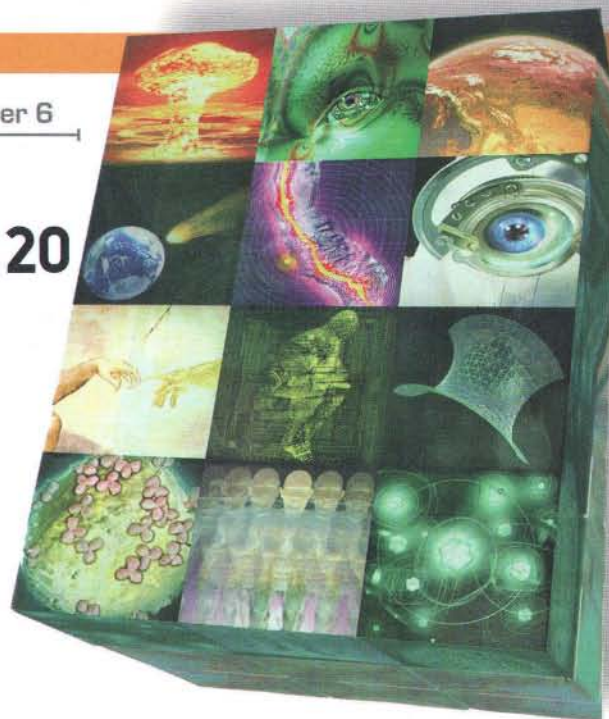
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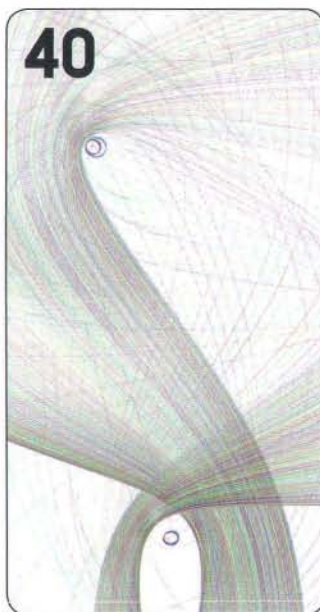
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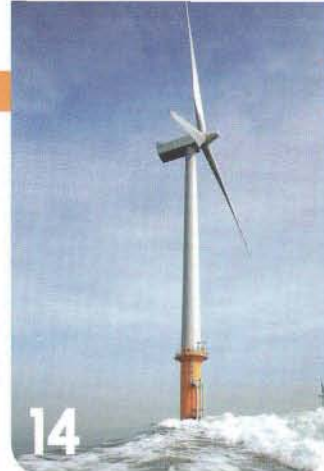
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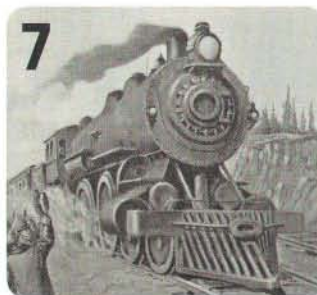
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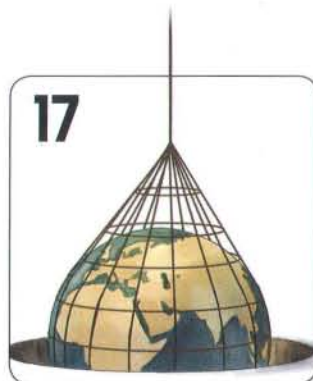
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those tasks are to a polished publication. Rather, one of our critical roles for readers is that we keep up with what's happening in science, enabling *Scientific American* to be the authoritative source for the information that matters to our audience. We go to conferences and meetings, pore over other publications, and routinely confer with our researcher sources and authors. As editors, we think short-term—what's the news that readers need to know right now, in a given issue?—and we also consider the longer view about what will come about in the months ahead.

In addition to reacting to news as it breaks, in other words, we work to *anticipate* what will happen. Case in point: the cover story for this issue, “12 Events That Will Change Everything.”

One day Phil Yam, the chief news editor, and I were having a routine planning discussion. So that our news team would always be in ready-to-respond mode, he told me, he was tracking the progress of a number of fascinating developments, such as the creation of life in the lab, all of which would have huge implications when they actually happened. Some of the events would unfold in surprising ways that most people didn't currently appreciate or expect. Did I think the editors would be interested in such a list? By now you must have surmised my answer. I hope you find the stories in this special package, which starts on page 20, as thought-provoking as I do.

Speaking of momentous events, what if

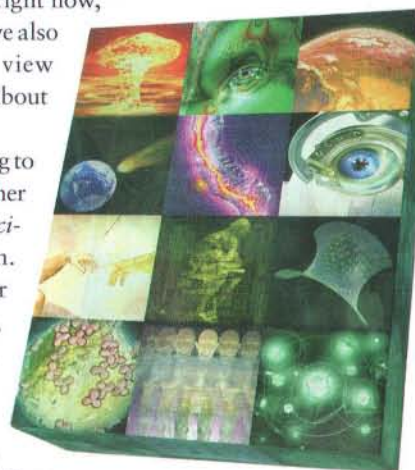
time were to vanish? How would our lives change? Not at all. Actually, physics tells us, time may always have been an illusion anyway. In his feature article, “Is Time an Illusion?” beginning on page 40, Craig Callender gives a helpful analogy. Time may be a kind of cosmic currency—a stand-in for other things we value, in much the same way that money is a placeholder that represents items of value in our transactions. Einstein's general theory of relativity conceptually may have wiped away the need for time in physics decades ago, but researchers are only properly incorporating that fact now. The notion of

time as illusion is somewhat controversial. Nevertheless, I think your experience of reading the article will be that it was time well spent.

While physicists debate the existence of time, eliminating something else—Alzheimer's disease—would have a much greater impact on the lives of individuals.

Its incidence has been climbing along with the graying of the population, and recent drug therapies have been disappointments, often because they were begun too long after the disease had wreaked its damage. Now new techniques that can track the disease before symptoms appear offer fresh hope for testing drugs at stages where they might be more effective, as senior writer Gary Stix tells us, starting on page 32. There's an event we can all look forward to.

**MARIETTE DICHISTINA**  
editor in chief





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## LETTERS

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### Fertilizers ■ Star Birth ■ Lobbyists



FEBRUARY 2010

#### ■ When Less Is More

The global challenge of addressing sustainable use of nitrogen fertilizers is well characterized in “Fixing the Global Nitrogen Problem,” by Alan R. Townsend and Robert W. Howarth.

Where the authors fall short, however, is in considering some of the solutions that agricultural research and innovation offer to address these problems. Conventional breeding and biotechnology are being applied to improve crop utilization of available nitrogen, thus reducing fertilizer demand without sacrificing increased yields. And best practices today, through the use of urease and nitrification inhibitors, minimize off-target movement of nitrogen by reducing evaporation and by maintaining fertilizer nitrogen in the ammonium form, which is less mobile and more efficiently utilized by many crops.

Technology and innovation, combined with intelligent public policy to promote more timely development and adoption, will be the foundation for sustainable solutions allowing the world to continue reaping the benefits of the Haber-Bosch process.

Michael Shaw and Cliff Gerwick  
Dow AgroSciences  
Indianapolis

#### ■ Fill In the Colors

In “Seeing Forbidden Colors,” Vincent A. Billock and Brian H. Tsou review work by Hewitt D. Crane and myself extensively

### “One man’s pork is another man’s vital national program.”

—Robert R. Rose WOODBRIDGE, VA.

and propose that our results and their replication of the forbidden-colors studies require a new winner-take-all alternative to well-established opponent-color theory. Neither Crane nor I ever posited that our findings of forbidden colors violated or even undermined color-opponent theory. In fact, we felt that our results told us nothing about color opponency in the retino-cortical pathways but much about how the visual mechanisms of the brain processed information once received. Our forbidden colors were neither “parlor tricks” nor hallucinations but the result of a series of experiments that explored the parameters of the “filling-in” mechanism.

Filling in, which functions across both naturally occurring stabilized images and artificially stabilized images, seems to “paint” colors and patterns across areas of the visual scene for which there are apparently no signals emanating from the retina. Our research showed that the color of the filled-in area appears to be determined by chromatic contrast at the perceptual boundary of the stabilized region. When we provided conflicting information at that boundary—for example, red on one side and green on the other—the filling-in mechanism “painted” both colors across the perceptual field. These results and others from our laboratory suggest that the filling-in mechanism functions according to its own rules, independent of color-opponent retino-cortical pathways.

Thus, there seems to be no need to propose a new color-opponent mechanism,



because even such a mechanism cannot explain how we see colors where the retina sends no neural signals to higher centers, for example, at the optic nerve head and in the shadow of the many retinal blood vessels.

Thomas P. Piantanida  
Greenleaf Medical  
Palo Alto, Calif.

## ■ Cold and Dark

It seems odd that in the recent article "Cloudy with a Chance of Stars," in which Erick T. Young discusses formation of massive stars, no mention is made of the potential role of cold dark matter or the alternative theories of modified Newtonian dynamics (MOND). The inadequacy of Newtonian gravity based purely on baryonic mass in describing the physics of galaxies has been well covered in *Scientific American*. One would think that the additional gravitation provided either by dark matter or by MOND would be significant in the formation of massive stars. Can Young explain why these important effects are ignored in the models he has described?

Robert Olshansky  
Wayland, Mass.

**YOUNG REPLIES:** Cold dark matter (CDM) has become an important component in current cosmological theories. Evidence for cold dark matter comes from observations of the rotation curves of galaxies and of the structures seen at galaxy and larger scales (bigger than 100,000 light-years, say). The lumpiness seen at smaller scales does not seem to require CDM, though. For star formation as discussed in the



**INTERSTELLAR CLOUDS (red and black) coalesce into stars, mostly under the gravitational self-attraction of the ordinary matter they contain. Dark matter tends to not concentrate in stars and instead flies right through them as it orbits the galaxy.**

article, we are looking at size scales of only one light-year or smaller. On these scales, ordinary matter seems to be all that is needed to explain the dynamics and energy balance of the structures we see. Also, because CDM does not interact strongly with electromagnetic radiation, it cannot radiate its energy efficiently. It is this radiation and cooling that tips the balance in favor of gravity to form stars.

## ■ Dancing until Dawn

Every lobbyist in Washington would dance until dawn if the proposal advanced by Jeffrey D. Sachs in "Fixing the Broken Policy Process" [Sustainable Developments] to forbid campaign contributions by registered lobbyists came to pass. Because these contributions come out of the lobbyists' own pockets, they would instantly receive, in effect, a raise. The step would make not a ripple in the corruption inherent in our current political campaign financing system. Contributions from lobbyists are a tiny share of the cash flowing in from moneyed interests and indeed from average Americans. Only mandatory campaign-spending limits offer any real hope of reducing the impact of money on Congress; a ban on television advertising would not hurt. Sadly, our Supreme Court is moving exactly in the opposite direction, clearing the way for unlimited third-party spending on elections.

The fundamental ingredient that is lacking is public consensus. And for that we have ourselves and our neighbors to blame. Farmers like corn ethanol, miners like coal, bankers like carbon trading, and so on. As my old boss once said, one man's pork is another man's vital national program. With such a diverse country, it is a wonder that anything gets done right.

My radical proposal: less money, certainly, but radically less; more lobbyists, not fewer, so that all our myriad points of view are better represented; more closed meetings so members could actually compromise in the public interest without fear of "gotcha" attacks from the interests hurt thereby.

Robert R. Rose  
Woodbridge, Va.

**ERRATUM** In "Comparatively Easy" [Perspectives], the editors referred to the "National Institute of Medicine." The correct name is Institute of Medicine of the National Academies.

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## Man in Space • Flight in Court • Pungent River

Compiled by Daniel C. Schlenoff

### JUNE 1960

**STUNT MAN**—"Putting a man in space is a stunt: the man can do no more than an instrument, in fact can do less." So said Vannevar Bush, chairman of the Board of Governors of the Massachusetts Institute of Technology, in a statement to the House Committee on Science and Astronautics. "There are far more serious things to do than to indulge in stunts. As yet the American people do not understand the distinctions, and we in this country are prone to rush, for a time, at any new thing. I do not discard completely the value of demonstrating to the world our skills. Nor do I undervalue the effect on morale of the spectacular. But the present hullabaloo on the propaganda aspects of the program leaves me entirely cool."

### JUNE 1910

**CURATIVE**—"Nearly all mineral waters have been found to contain radioactive emanation. The tracing of efficacy to radioactivity naturally suggested the artificial control of radioactivity so as to impart curative effects to inactive spring water or to increase the efficiency of natural springs. The idea of adding variable amounts of emanation has been carried into practice on a large scale by the Administration of the Municipal Salines of Kreuznach, Germany, where drinking and bathing water, artificially treated by the very radioactive substances contained in the springs, is manufactured and sold. Though the radium-water cure is yet of too recent date to allow definite conclusions to be drawn, it doubtless constitutes a valuable addition to the present methods of modern medicine."

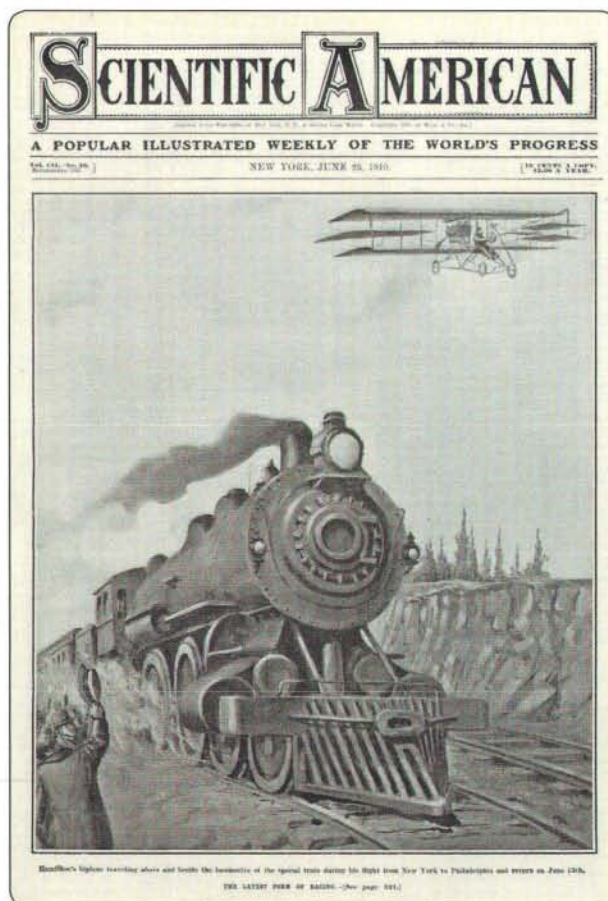
**LEGAL FLYING**—"In dissolving the injunction granted in favor of the Wright brothers against Curtiss, by Judge Hazel, and the similar injunction granted by Judge Hand against Paulhan, the Circuit Court of Appeals has simply followed a long-established precedent in patent law. Curtiss at least was a successful aviator before the Wright brothers decided to cast aside all secrecy and to show the world what manner of machine was that of whose performances they had darkly hinted. Blériot, too, had been pluckily experimenting for some time before the Wrights flew in public. It is astonishing that the lower court should have failed to find in these facts a sufficient conflict of evidence to deny the

granting of an injunction. With the reversal of the decision of the lower court by the Circuit Court of Appeals, the development of aviation in this country is now unhampered."

**THRILLING RACE**—"Aviator Charles K. Hamilton made a daring and thrilling flight from New York to Philadelphia. The flight was planned by the New York Times and the Philadelphia Public Ledger, and aviator Hamilton, carrying a letter from Mayor Gaynor of New York to Governor Stuart of Pennsylvania, executed that flight on schedule time. During a considerable part of the trip he raced a special train which at times found difficulty in keeping up with him [see illustration]."

### JUNE 1860

**WHIFFY THAMES**—"Last year, during three months of very dry weather, old Father Thames—that once classic stream—became a huge sewer, sending forth foetid odors over all the British metropolis. A report recently presented on the subject contains the statement that about \$88,000 worth of deodorizing material was thrown into the Thames during the months of June, July and August, chiefly chloride of lime, of which 478 tons were used, and chalk lime, of which 4,280 tons were used. These were chiefly thrown into the sewers, and while the temperature of the river remained high—from 69 to 74 degrees, the river remained proof against all efforts of deodorization. Great preparations have been made this year to provide a sufficient supply of the perchloride of iron in order to modify the pungent powers of Father Thames' snuff-box."



**AVIATION SPEEDS AHEAD**—Charles K. Hamilton races the iron horse in his Curtiss-type biplane, 1910



## Research &amp; Discovery

## Fossils of Our Family

A new human species is identified, but does it belong on the line leading to *Homo sapiens*? BY KATE WONG

FOSSILS OF A HUMAN SPECIES NEW TO SCIENCE COULD BE the direct ancestor of our genus, *Homo*. Discovered in Malapa Cave, located some 40 kilometers outside of Johannesburg, South Africa, the finds comprise two partial skeletons that are nearly 1.95 million years old. The researchers have named them *Australopithecus sediba*.

The pair—an adult female and juvenile male that may have been mother and son—appear to have fallen through a hole in the cave ceiling while possibly attempting to access a pool of water inside. So exceptional is the preservation of the skeletons that the discovery is being likened to the famous Lucy fossil from Ethiopia. But the startling mix of primitive and advanced traits evident in the remains is sparking debate over where the new species belongs on the family tree.

Considering the virtually nonexistent fossil trails of our cousins the chimps, bonobos and gorillas, the human fossil record is extraordinary. There are, however, significant gaps in researchers' knowledge of how we came to be. One such blind spot is the origin of *Homo*. Most experts agree that our genus evolved from a species of *Australopithecus*—either *A. afarensis* (Lucy's species) or *A. africanus*. Connecting the dots between one of these *australopithecine* species and *Homo* has been difficult, however, because the oldest known *Homo* remains are so few and fragmentary.

Scientists have supposed that *Homo habilis*, which lived between 2.3 million and 1.5 million years ago, signaled the debut of *Homo* and subsequently gave rise to *H. erectus*, the first hominin (member of the human lineage) to spread out from Africa across the globe and the one thought to have spawned later human species, including *H. sapiens*.

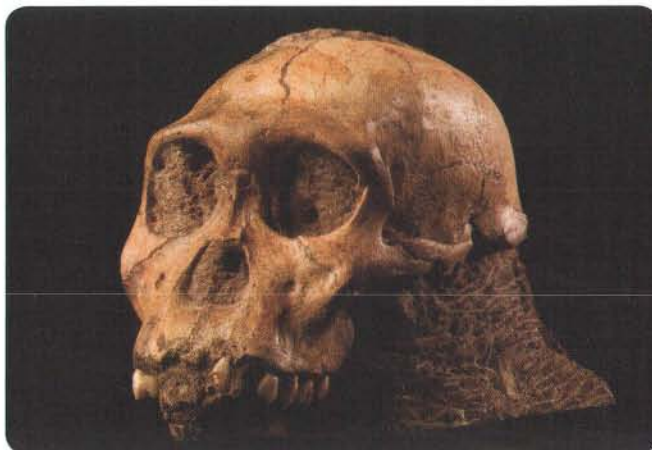
Enter *A. sediba*. In a paper describing the fossil remains in the April 9 *Science*, Lee Berger of the University of the Witwatersrand in Johannesburg and his colleagues suggest that *A. africanus* gave rise to *A. sediba*, which in turn gave rise to *Homo*. Intriguingly, the team hints that *A. sediba* might even be more closely related to *H. erectus* than *H. habilis* is, thus potentially relegating *H. habilis* to a side branch of the family tree, rather than a coveted spot on the line leading to us.

Berger and his collaborators based their conclusions on *A. sediba*'s distinctive amalgam of primitive and advanced traits. Features such as small brain size, slight build and very long arms link the creature to the australopithecines, especially *A. africanus*. Yet the new species also exhibits a number of characteristics seen only in *Homo*, including its flatter face, robust pelvis and long, striding legs.

Other paleontologists have praised the discovery but are

divided on the issue of how to classify the new hominin. "The proposed link between *A. sediba* and early *Homo* is forced and tenuous at best," asserts William L. Jungers of Stony Brook University, noting that alleged skeletal similarities are not very compelling.

A different take comes from William H. Kimbel, director of the Institute of Human Origins at Arizona State University, who argues on the basis of the advanced features of the face and pelvis that the new fossils "probably belong in the *Homo* genus." They do not illuminate its origin, however. Kimbel points out that a site where he works in Hadar, Ethiopia, has yielded a *Homo* specimen that predates the *A. sediba* fossils by hundreds of thousands of years.



RELATIVE OF OURS? *Australopithecus sediba* is a previously unknown member of the human family that may be ancestral to *Homo*.

Exactly how the skeletons relate to known *Homo* species is difficult to establish given the paucity of early *Homo* remains, observes paleoanthropologist Susan C. Antón of New York University. She suspects that *A. sediba* may be a dead-end branch of *Homo*, rather than an ancestor of later species such as *H. erectus*.

Berger, for his part, contends that regardless of whether *A. sediba* ends up in the family tree, the fossils open a much needed window on the evolutionary processes at work during a poorly understood interval of human evolution. For instance, the morphological mosaic evidence in the skeletons shows that different parts of the body were changing at different times—the legs changed before the arms, and the pelvis changed before the brain.

Further insights may not be far off: Berger says he has found





at least two more hominin skeletons in the cave. He is currently excavating them and has assembled a team of about 60 experts to analyze all of the material from the site in detail. Their to-do list includes

**FOSSIL REMAINS OF *A. sediba* include parts from two skeletons that exhibit a mix of primitive and advanced traits.**

determining whether the fossils might contain proteins or DNA suitable for sequencing, reconstructing the environment the hominins lived in, and studying differences between males and females. Such efforts will no doubt reveal an incredibly detailed portrait of this newest addition to the human family.

## A Simple Twist of Fate

Old "twistor" idea from Roger Penrose ignites the latest superstring revolution **BY GEORGE MUSSER**

IN THE LATE 1960S THE RENOWNED UNIVERSITY OF OXFORD physicist and mathematician Roger Penrose came up with a radically new way to develop a unified theory of physics. Instead of seeking to explain how particles move and interact within space and time, he proposed that space and time themselves are secondary constructs that emerge out of a deeper level of reality. But his so-called twistor theory never caught on, and conceptual problems stymied its few proponents. Like so many other attempts to unify physics, twistors were left for dead.

In October 2003 Penrose dropped by the Institute for Advanced Study in Princeton, N.J., to visit Edward Witten, the doyen of today's leading approach to unification, string theory. Expecting Witten to chastise him for having criticized string theory as a fad, Penrose was surprised to find that Witten wanted to talk about his forgotten brainchild.

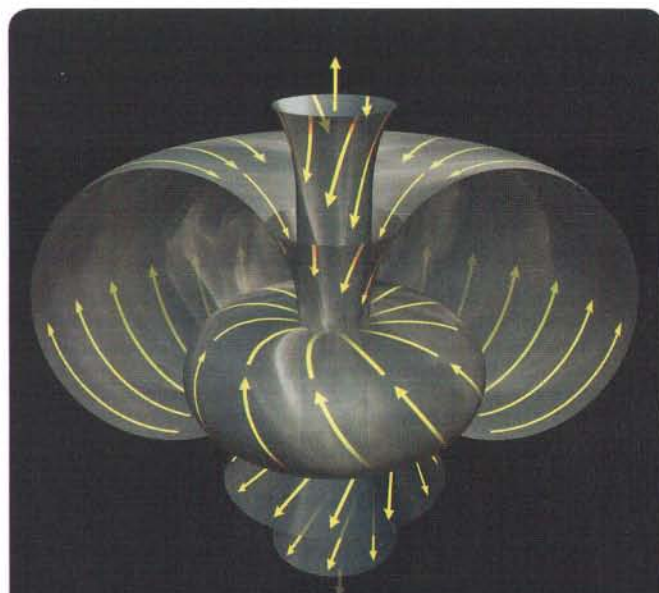
A few months later Witten posted a dense 97-page paper that tied together twistors and strings—bringing twistors back to life and impressing even the harshest critics of string theory. In the past few years theorists have built on Witten's work and rethought what space and time are. They have already spun off calculational techniques that make child's play of the toughest problems in ordinary particle physics. "I have never been more excited about physics in my life," says string theorist Nima Arkani-Hamed, who recently moved to the institute from Harvard University to immerse himself in the emerging field. "It is developing at a blistering pace right now, with a group of roughly 15 people in the world working on it day and night."

Prior to Witten's work, twistorians and string theorists moved in separate circles and spoke what might as well have been different languages. Whereas Penrose and his colleagues have made their names studying Einstein's general theory of relativity, string theorists trace their descent to particle physics. Lionel Mason of Oxford says that when he and Penrose visited Syracuse University in 1987, they blew off a talk on string theory that, in hindsight, would have given them the clues they needed. "We didn't go to a particle physics seminar—we were relativists," he says.

Penrose's original goal was to reconsider how quantum principles apply to space and time. Conventional wisdom held that spacetime geometry should fluctuate on quantum scales, alter-

ing how events relate to one another. But in that case, an event that was supposed to cause another may no longer do so, creating paradoxes such as those found in time-travel stories. In twistor theory, causal sequences are primary and do not fluctuate. (The theory gets its name from what causal relations look like around a spinning particle, as shown at the left.) Instead the location and timing of events fluctuate. But twistorians could not make this idea precise—until string theorists showed that an event of ambiguous location and time is nothing more or less than a string.

String theorists, for their part, had a promising idea for the creation of space that they could not get to work. In 1997 they conjectured that particles zipping around in four dimensions can behave just like strings interacting in five dimensions. The new dimension materializes like a figure in a pop-up book. Yet this



**TWISTORS**, which many physicists think may represent a level of reality underlying space and time, describe a particle as a contorted pattern of light rays (a so-called Robinson congruence).



conjuring trick produced only a single dimension of highly warped space. Using twistor concepts, theorists have now shown how all the dimensions of ordinary space—and even time—can pop out.

Many theorists find it quite natural that spacetime would be derivative. Andrew Hodges of Oxford points out that we do not perceive spacetime directly; we infer that events happen in specific locations at specific times from the information that comes to us. “This idea of points of spacetime as being primary objects is artificial,” he says. Indeed, the concept of distinct positions and times breaks down because of the gravitational warping of spacetime and the notoriously spooky connections between quantum particles.

Whether or not they succeed in remaking space and time, twistorians and string theorists have already endeared themselves to particle physicists. Even fairly simple particle collisions demand equations containing tens of thousands of terms, which are written using a strategy devised by the famous physicist Richard Feynman in the 1940s. Almost all of those terms end up canceling out, but you don’t know in advance which will cancel, so you have to slog through all of them. An alternative strategy inspired by twistors and strings captures symmetries that Feynman’s approach does not, so it sheds the excess mathematical baggage from the outset. Calculations that math whizzes once gave up on now take just a couple of weeks. “I’m pretty sure Feynman would be quite pleased if he saw what we can do,” says Zvi Bern of the University of California, Los Angeles.

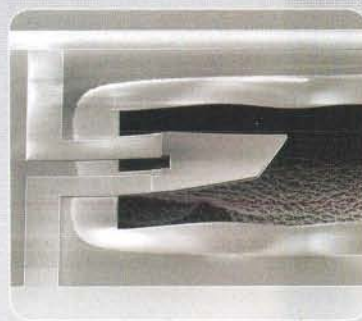
The emerging theory of spacetime is still very tentative and so mathematically dense that even those physicists directly involved admit they can barely follow what is going on. Theorists have yet to explain why, if spacetime is merely a construct, it nonetheless seems so real to us. It must somehow take shape much as life springs from inanimate matter. Whatever the process is, it cannot occur only on subatomic scales, because the concept of size must itself emerge. It should be evident on all scales, everywhere around us, if only we know how to look.

## “Quantum Microphone” Puts Visible Object in Two Places at Once

What is the sound of one molecule clapping? Researchers have demonstrated a device that can pick up single quanta of mechanical vibration similar to those that shake molecules during chemical reactions and have shown that the device itself, which is the width of a hair, acts as if it exists in two places at once. This type of “quantum weirdness” feat so far had only been observed at the scale of molecules.

“This is a milestone,” says Wojciech Zurek, a theoretical physicist at Los Alamos National Laboratory. “It confirms what many of us believe, but some continue to resist—that our universe is quantum to the core.”

Aaron O’Connell, a graduate student at the University of California, Santa Barbara, used computer-chip manufacturing techniques to create a mechanical resonator—akin to a small tuning fork. It was one micron thick and 40 microns long, just big enough to be visible with



**DEAD OR ALIVE?** This 40-micron-long resonator is the largest object seen in two places at once.

the naked eye. He and his collaborators then attached the resonator to a superconducting circuit and cooled everything to within 0.025 of a degree above absolute zero. At those temperatures, the resonator would either be completely still or possess a quantum of vibrational energy, called a phonon. Vibrations could be detected using the superconducting circuit—in which case the device acted as a “quantum microphone.” Alternatively, running currents in the circuit would force the resonator to vibrate in sync. Thus, when the team put the circuit into a superposition of two states, one with a current and the other without, the resonator was in a superposition of vibrating and not vibrating. In a vibrating state each atom in the resonator moved only by an extremely small distance—less than the size of the atom itself. Thus, in the superposition of states the resonator was never really in two totally distinct places. But still, the experiment showed that a large object (made of about 10 trillion atoms) can display just as much quantum weirdness as single atoms do. O’Connell presented the results in March at a meeting of the American Physical Society, and the findings appeared in the April 1 *Nature*. (*Scientific American* is part of Nature Publishing Group.)

—Davide Castelvecchi

## Expert Education

A field study tries to see how expertise can be taught to novices

BY CHARLES Q. CHOI

DEATH VALLEY, CALIF.—THE DOZEN STUDENTS and scientists spread over an area called Furnace Creek look like cyborgs in floppy hats scrabbling over the boulders. They inspect rocks with magnifying lenses held up to eyeglasses sporting miniature cameras and infrared lights, then hammer chips off them.

A seasoned geologist could tease out a history of earthshaking clashes from evidence in the terrain here. A break in a steep gray slope, for instance, suggests a fault at work fracturing the landscape. The aim now of these cameras is to see

how researchers’ eyes dart across this scene, to understand how experienced minds unconsciously scan the world for clues that point the way to discoveries. The hope is that one day scientists will be able to train neophytes with virtual-reality displays that simulate environments of interest.

“We know a lot about how to educate people on facts, but we know almost nothing about how to educate people on acquiring perceptual skills other than lots of repetition, which can be very time-consuming and expensive,” says cognitive scientist



Robert A. Jacobs of the University of Rochester. "It would be great to develop more effective training procedures." Such research could go well beyond geology, too, and delve into how detectives analyze crime scenes or soldiers look for camouflaged targets.

For teaching geologic expertise in Death Valley—where the driest, hottest and lowest places on the continent are found—the key is a wearable eye-tracking device that can monitor what people look at in a natural environment. It consists of two lightweight video cameras mounted on eyeglass frames—one pointed at what a person is seeing, the other pointed at the person's right eye—tracking its movements with the help of a little infrared LED that shines an invisible beam onto the eye. Two camcorders in a slim backpack record data that eye-tracking programs then process later.

The novice and seasoned geologists from the University of Rochester have gone out with the eye trackers about four times a day over their two-week field trip across California, which took them from San Francisco by the San Andreas Fault through the snowy Sierra Nevada near Yosemite National Park to the harshest area of the U.S. "Death Valley is a great place, where one can really see active geology firsthand—forces that are shaping the crust of the earth," says geophysicist John A. Tarduno, another of the Rochester scientists. "Most people think of Death Valley as this big hole because it's below sea level, and that's true at the heart of it, but right adjacent is an 11,000-foot mountain."

Nature does not like such elevation differences right next to one another; erosion tends to even things out. "The fact we have a valley today hints at active processes to maintain that difference," Tarduno explains. "It is conclusions like these that we hope to see students reach by themselves."

As with almost all field trips, unexpected troubles arose, such

as the sandstorm that engulfed Death Valley on the first day, which sent the group to a campground at the snowline of Mount Whitney, the highest point in the contiguous 48 states. The desert is trouble in other ways—the glint of the sun off the eye can confuse the eye-tracking software, which is why the experimenters donned ungainly wide-brimmed sun hats. Even so, the software loses track of gaze in about 10 to 15 percent of the video

frames the cameras record, a problem future algorithms might fix.

Aside from the eye trackers, the researchers also used a robot-operated camera to take hundreds of high-resolution photographs of the areas, which will later get stitched together for panoramic images displayed on giant wraparound screens. "The hope is we verify that student geologists in the field and those surrounded by these virtual environments view formations the same way so we can use simulations to train novices on dozens of virtual field trips, cutting down on the costs of travel and equipment to make better use of actual trips," says imaging scientist Mitchell R. Rosen of the Rochester Institute of Technology.

Those flashes of discovery are what the researchers are seeking to record now. At the Long Valley caldera, Tarduno quizzes students about the lava flows they have seen and the curve of surrounding landmasses until they realize they are standing in a dormant supervolcano roughly 20 miles long, 11 miles wide and covered in snow. "I was really excited at that in-

stant," student Shannon Moss recalls. "I saw this circle we were in, and it just came to me." An otherwise fleeting moment now captured by the eye trackers.

*Charles Q. Choi is a frequent contributor based in New York City.*



**EYES FRONT:** The eyeglasses of geologist Yoichi Usui of the University of Rochester have cameras mounted on them to capture his view and his eye movements.

## Medicine & Health

# Adoption Agents

Debate on how to keep big pharma interested in orphan drugs **BY JESSICA WAPNER**

SINCE ITS PASSAGE IN 1983, THE ORPHAN DRUG ACT (ODA) HAS led to the approval of 357 drugs for rare diseases and a pipeline of more than 2,100 additional products. Before the ODA, just 10 such drugs existed. Considering that some 7,000 rare diseases affect 20 million to 30 million Americans, federal overseers and

patient advocates are anxious to ramp up efforts even more. But finding a way to give the act a second wind is kicking up dust both scientific and financial.

The U.S. passed the ODA as a way to encourage pharmaceutical firms to develop treatments for uncommon illnesses—those



affecting no more than 200,000 Americans. The act hinges on financial incentives, including federally funded grants and contracts for clinical trials, a 50 percent tax credit on trial costs and, above all, seven years of market exclusivity starting from the date of drug approval. (Nonorphan drugs receive patent protection, a more cumbersome and potentially less profitable arrangement.) The law has enabled researchers and manufacturers to invest in drugs otherwise unlikely to turn a profit because of the limited need.

But these provisions still do not cast a wide enough net. Peter Saltonstall, president of the National Organization for Rare Diseases, a patient advocacy group, claims that a company recently cited financial reasons for dropping a promising drug for a disease affecting 1,500 people nationwide. (Saltonstall declined to name the disease.) Diseases affecting even fewer people—and there are plenty of them—have even less of a chance.

Tim Coté, head of the Food and Drug Administration's Office of Orphan Products Designation, acknowledges that there is no easy answer. Coté, whose office decides whether a new product warrants orphan designation, is also troubled by the persistent unwillingness of big pharma to focus on rare diseases. "They frequently come out with press releases saying how important orphan products are to them," he says. "And they infrequently pass anything substantive over my desk."

To woo industry giants and ease the process for already committed smaller companies, the 2010 FDA appropriations bill has charged Coté's office with reevaluating the review process for orphan drugs. As Coté explains, alternative statistical models (such as Bayesian design) may allow investigators to shrink trial size without jeopardizing safety and efficacy—basically, developing the ability to glean

more insight from fewer data. These designs have yet to be implemented on a wide scale, but Coté emphasizes the FDA's flexibility when it comes to orphan drug studies. The compound PEG-ADA, which treats severe combined immunodeficiency—also known as bubble boy disease—



**ORPHAN SUCCESS:** Once only for rare conditions causing spasms, Botox, given via injection, is now an antiwrinkle blockbuster.

received FDA approval based on case studies with just 12 patients.

Coté also hopes to generate interest in orphan product development through new on-site workshops. These sessions, the first of which was held recently in Claremont, Calif., provide practical guidance about the ODA's financial incentives and how to file an orphan drug application.

Still, cost issues loom. Orphan drugs are expensive to produce, and prices need

to be set high to recoup costs within such a small market. The ODA's exclusivity period also means drugmakers can price drugs at whatever the market will bear. And they can reap huge benefits if an orphan drug becomes a blockbuster, as happened with Botox, initially created to treat

two rare conditions that cause eye and neck muscle spasms. In contrast, the European equivalent of the ODA includes a provision for revisiting orphan status in such cases. Similar proposed amendments to the ODA, approved by Congress in 1990, were vetoed by President George H. W. Bush, citing concern that the new measures would stifle innovation.

Coté sees no problem with drugmakers earning an unexpected bonanza from their investment. "The ODA is very single-minded in terms of driving innovation for the treatment of rare diseases," he says. "If larger populations end up benefiting from those inroads made for rare diseases, then so what?"

Still, orphan drugs, which cost up to \$600,000 a year, may end up driving a broader discussion of how much is too much. This is an issue "that society is going to have to deal with," says Mike Scott, who serves on the board of directors of the International Myeloma Foundation. "And that has commercial implications, research implications and societal implications."

As Coté sees it, the focus should be on getting orphan drugs made, whatever the cost, to repay a long overdue debt. Rare diseases have led to a host of medical knowledge, including the urea cycle, metabolism and blood clotting. "We owe people with rare diseases some therapies," he argues, "because most of our understanding in medical science is based on rare diseases."

*Jessica Wapner, based in New York City, often writes about biomedical issues.*



# Bad Wraps on Viruses

A possible broad-spectrum antiviral acts by damaging lipid coats **BY BOB ROEHR**

BENHUR LEE MAY HAVE DISCOVERED A medical silver bullet—one that can disable HIV, the exotic Ebola virus, the common flu and possibly every kind of enveloped virus on the planet.

Working from his laboratory at the University of California, Los Angeles, Lee came across this bullet after first creating a hybrid virus, one that combined the envelope (or outer surface) of the deadly Nipah virus and the core of the benign vesicular stomatitis virus. The hybrid can infect cells but cannot replicate in them.

He then screened a library of 30,000 compounds for activity against the hybrid's envelope to see if they inhibited entry into the cell. One compound, called LJ001, "looked really good," Lee recalls, and it wasn't toxic to cell cultures.

After a series of studies confirmed the activity and lack of toxicity, Lee sent samples of the compound to the Galveston National Laboratory at the University of Texas Medical Branch, which has biosafety labs for testing against whole Nipah, Ebola and other deadly viruses. Amazingly, LJ001 inhibited viral entry of all of them. Lee later pitted it against HIV—it

worked there, too. He continued testing the compound against more viruses until the list reached 20—all successes.

Additional experiments revealed that the compound failed against an entirely different class of viruses. At that point, Lee figured out LJ100's secret: it works only against viruses that have lipid envelopes, which also happen to be the most deadly ones.

The compound evidently binds to lipids in the envelope of both the virus and human cells, causing damage to both. The difference is that the cell can repair all kinds of regularly occurring insults; the genetically simpler virus has no repair mechanisms. (Newly created viruses get their lipid coats by literally ripping them off the cell membrane as they bud from infected cells.) Once the viral lipids were disabled by LJ001, they stayed that way. Lee's first paper on the compound's antiviral activity appeared in the February 16 *Proceedings of the National Academy of Sciences USA*.

Virologist Warner C. Greene of the University of California, San Francisco, finds the work fascinating but cautions that



**ADENOVIRUSES** and others that have a lipid coat could be neutralized by one compound.

"from a therapeutic point of view, it is a very, very early finding." He notes that the membrane disruption may be more toxic than is currently appreciated. "Primary cells often are much more sensitive than laboratory-adapted cells," Greene says.

Lee certainly hopes to find out. He is currently working with others at U.C.L.A. to turn the promising compound into an actual drug, which would have more going for it than just a broad-spectrum ability. "I can't imagine how the virus can develop resistance to this type of drug," Lee says.

*Bob Roehr is based in Washington, D.C.*

## Energy & Environment ■■■■

### Traffic Avoided

Predictive modeling warns drivers an hour before jams occur **BY MARK FISCHETTI**

ONBOARD NAVIGATION AND MOBILE APPLICATIONS CAN TELL drivers how to avoid traffic jams. Trouble is, most of the drivers are already on the road, perhaps already in the jam. But IBM is about to deploy a system that will predict traffic flow up to an hour before it occurs, giving travelers ample time to avoid trouble.

During pilot tests in Singapore, forecasts made across 500 urban locations accurately predicted traffic volume 85 to 93 percent of the time and vehicle speed 87 to 95 percent of the time. Similar results were achieved in Finland and on the New Jersey Turnpike.

The key to success is predictive modeling—software that combines real-time data from road sensors and cameras, as well as

GPS transponders in taxis, with historical traffic information, roadwork conditions and weather forecasts. Each week the model recalibrates based on statistics from the most recent six weeks. It broadcasts advisories to electronic road signs and car navigation displays. The system also predicts when a congested road will return to normal flow.

IBM has signed contracts with two U.S. transportation authorities to deploy a full system, according to spokesperson Jenny Hunter. The locations will be announced soon. Singapore may commit as well and is also testing a variation that will predict bus arrival times for riders waiting at bus stops.



In each location, ongoing work will optimize the advisories. If, for example, Highway 1 is clogged and too many drivers who receive messages flock to Highway 2, it will become clogged; engineers will customize the model so it can determine whether sending the messages to only 25 or 40 percent of drivers, say, would best balance the two roads. And because a high percentage of drivers now carry cell phones, IBM is working with several telecom companies to be able to track the continually changing density of their phones along roadways, which could provide finer-grained modeling. To protect privacy, the identity of individual phones would not be disclosed.

The company has also announced its intention to develop services that could tell individual subscribers ahead of time which of various routes would get them to their preselected destination fastest, given current conditions. Voice recommenda-

lyzes the person's HIV genotype and his or her current health characteristics against an evolving database of treatment outcomes for more than 33,000 patients and 98,000 therapies. Similar applications might determine which type of breast or prostate cancer treatment could benefit a patient most.

IBM is also working with the Washington, D.C., Water and Sewer Authority to

predict in real time where problems are likely to arise—such as which sewer lines might flood during storms. The goal is to adjust valves ahead of time, systemwide, to minimize overflows and to deploy maintenance crews to specific locations early. In March, IBM opened a predictive analytics lab in Xi'an, China, to help business clients such as Xi'an City Commercial Bank anticipate customer trends before they occur.



**BACKUP PLAN:** A new service from IBM would predict congestion up to 60 minutes ahead of time and suggest alternative routes.

tions would be sent to a person's vehicle navigator or cell phone.

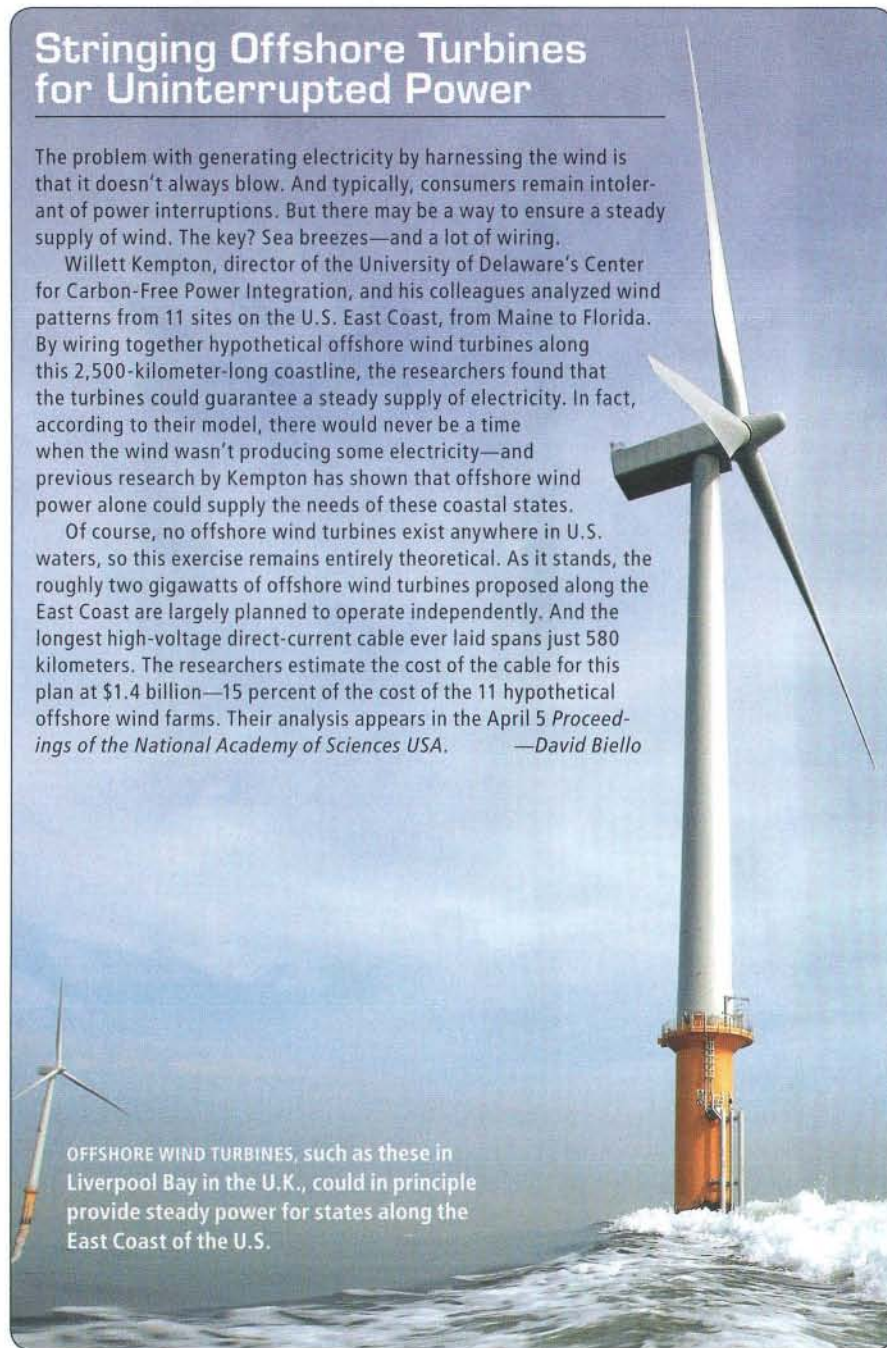
Similar analytics are being applied to other applications. "The beauty of predictive modeling is that it translates across disciplines," says Robert Morris, IBM's vice president of service research in Armonk, N.Y. For example, the company's laboratory in Haifa, Israel, is testing a program called EuResist that predicts the success of different drug cocktails for an HIV patient over time. The software ana-

## Stringing Offshore Turbines for Uninterrupted Power

The problem with generating electricity by harnessing the wind is that it doesn't always blow. And typically, consumers remain intolerant of power interruptions. But there may be a way to ensure a steady supply of wind. The key? Sea breezes—and a lot of wiring.

Willett Kempton, director of the University of Delaware's Center for Carbon-Free Power Integration, and his colleagues analyzed wind patterns from 11 sites on the U.S. East Coast, from Maine to Florida. By wiring together hypothetical offshore wind turbines along this 2,500-kilometer-long coastline, the researchers found that the turbines could guarantee a steady supply of electricity. In fact, according to their model, there would never be a time when the wind wasn't producing some electricity—and previous research by Kempton has shown that offshore wind power alone could supply the needs of these coastal states.

Of course, no offshore wind turbines exist anywhere in U.S. waters, so this exercise remains entirely theoretical. As it stands, the roughly two gigawatts of offshore wind turbines proposed along the East Coast are largely planned to operate independently. And the longest high-voltage direct-current cable ever laid spans just 580 kilometers. The researchers estimate the cost of the cable for this plan at \$1.4 billion—15 percent of the cost of the 11 hypothetical offshore wind farms. Their analysis appears in the April 5 *Proceedings of the National Academy of Sciences USA*. —David Biello



OFFSHORE WIND TURBINES, such as these in Liverpool Bay in the U.K., could in principle provide steady power for states along the East Coast of the U.S.



# Look, Ma—No Junctions!

A radically simpler transistor, 85 years after it was proposed **BY DAVIDE CASTELVECCHI**

THE TRANSISTORS AT THE HEART OF EVERY COMPUTER, TODAY numbering in the billions on a single chip, have generally been based on the concept John Bardeen, Walter Brattain and William Shockley first turned into a prototype at the Bell Labs in 1947. Physicists have now demonstrated a radically simpler transistor design, first patented by Austrian physicist Julius Edgar Lilienfeld in 1925 but never turned into a practical device until now. This simpler version could push computers to become faster and to consume less power.

In every transistor, an electrode, called the gate, governs whether current can run along a semiconductor strip, thereby defining an on or off state essential to a computer's binary function. Traditionally, the semiconductor strip is structured like a sandwich, with one type of material between two layers of another type. In the "off" position the sandwich acts as an electrical insulator, but the gate can turn it into a conductor, typically by creating an electric field. In chip fabrication the sandwich is obtained from a strip of silicon "doped" with other elements. For example, the middle section can be created by adding in atoms that tend to hog extra electrons; the side sections get atoms that tend to give electrons away. Each section separately could conduct electricity, but electrons will refuse to move across the middle section unless the gate is turned on.

The boundaries between consecutive sections are called junctions. As transistor size shrinks, it is becoming a challenge to produce sharp boundaries where doping concentrations change abruptly over distances of just nanometers, says Jean-Pierre Colinge of the Tyndall National Institute in Ireland.

A solution, then, is to eliminate those boundaries. Following Lilienfeld's idea, Colinge and his team have built a transistor with one type of doping only and thus no junctions. The new device is a one-micron-long nanorod of heavily doped silicon, with the gate crossing over its middle section. An electric field from the gate turns the transistor off by depleting that middle section of its electrons, preventing the flow of current through the rod. The team describes its result in the March *Nature Nanotechnology* (*Scientific American* is part of Nature Publishing Group).

An effective depletion of electrons requires the rod to be just 10 nanometers thick, a feat that has only recently become possible in large-scale manufacturing. "The device should be able to be integrated in silicon chips quite readily," because it is compatible with existing fabrication processes, Colinge says. The junctionless design is more effective at switching currents on and off, he says, which means it could work at lower voltages, producing less waste heat, and at faster speeds. (After increasing for decades, computer clock speeds have essentially been stuck at about three gigahertz for the past several years.)

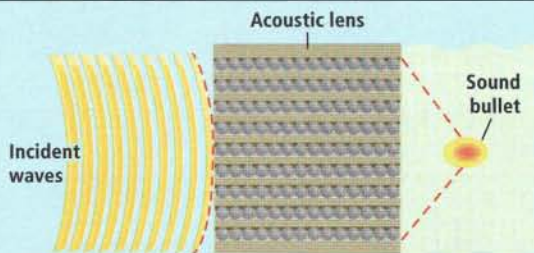
Thomas Theis, director of physical sciences at the IBM Watson Research Center in Yorktown Heights, N.Y., says that the junctionless transistor could be useful if the authors can make it much shorter than the current one micron, to better match existing components. Colinge says that shrinking it down to 10 nanometers should be feasible, and his team is working on getting there. Since the paper's publication, Colinge says, several semiconductor companies have shown interest in the transistor, perhaps getting ready to give new meaning to a future that has no boundaries.

## Acoustic Lens Turns Sound into Sonic Bullets

The manipulation of sound waves has led to critical technologies such as ultrasound imaging. Alessandro Spadoni and Chiara Daraio of the California Institute of Technology have now developed a new type of acoustic lens to make sound waves even more powerful.

Acoustic lenses focus sound in much the same way optical lenses focus light. Instead of using glass and mirrors, the duo designed an acoustic lens using 21 rows of 21 stainless-steel spheres. But instead of firing sound waves at the lens, they actually strike the first sphere in each row "so that we send a compressive wave down each stack or row," Spadoni explains. The researchers effectively tune the focal point of the lens by changing how hard they strike the lens (affecting the waves' amplitude) and the size of the spheres (affecting wavelength). The waves are then transmitted into an object, such as a human limb, where they focus down to a point.

The ability to focus could improve ultrasound imaging, according to Spadoni, who described the work online in the April 5 *Proceedings of the National Academy of Sciences USA*. Even more daring would be "sound bullets" for noninvasive surgical operations, the researchers say. Acoustic energy can heat tissue, an effect already used in hyperthermia therapy. The Caltech nonlinear acoustic lens could aid in the treatment of tumors by increasing the temperature of cancerous tissue to lethal levels without affecting healthy tissue. —Larry Greenemeier



**ACOUSTIC LENS**, consisting of rows of stainless-steel balls, can focus incident compression waves to a small area for better ultrasound imaging or even tumor destruction.



# Terror in a Vial

Bioweapons prevention needs to get more scientific

BY THE EDITORS

When envelopes containing the bacterial spores that cause anthrax started arriving in media offices and on Capitol Hill in the fall of 2001, a new era in biological warfare began. To pinpoint the source of the attacks, federal agents quickly sought out specialists to perform cutting-edge molecular fingerprinting on the ultrafine powdered spores. That evidence, which helped the government to finger a lone army scientist as the culprit, is now being reviewed by the National Academy of Sciences. Yet the essential lessons of the episode—that biological weapons are no longer just a battlefield risk and that innovative cooperation between law enforcement and science works—appear to have been forgotten already.

When it comes to countering the threat of biological weapons, most governments, including that of the U.S., are still mired in a decades-old nuclear-arms model geared toward preventing hostile nations from acquiring closely guarded weapons-making materials. It is an approach unsuited to the modern reality wherein non-state actors are more likely than states to use biological warfare agents and the growth of biotechnology is only making those weapons easier to come by. Security experts have long warned that would-be terrorists no longer need to steal deadly pathogens when commonplace genetic engineering techniques could turn a benign microbe into a killer or synthetic biology tools might be used to build a virus from scratch.

Now subversives no longer have to make their own weapons at all—they can find sources with ready-made material online. In “Fake Botox, Real Threat,” on page 66, Ken Coleman and Raymond A. Zilinskas point to a proliferation of international counterfeiters cashing in on the craze for the wrinkle-smoothing drug Botox, whose active ingredient botulinum neurotoxin is one of the deadliest poisons on earth. Many of the sales take place through Web sites, and most of the counterfeits contain real toxin, meaning that basement brewers may already be cultivating lethal toxin-making bacte-

ria to satisfy avid consumer demand. The authors ask, What is to stop those criminals from simply selling pure toxin to terrorists instead? In fact, what is to stop terrorists themselves from getting into the bootleg Botox business, for profit and easy access to toxin?

The problem is not limited to botulinum toxin. In January a report from the Henry L. Stimson Center policy think tank in Washington, D.C., noted that other items on the government’s “select agent” list of potential bioweapons, such as ricin and tetrodotoxin, are also being developed as pharmaceuticals to treat cancer and relieve pain. If one of these new drugs becomes wildly popular, will yet another select agent inspire a new wave of illicit Internet entrepreneurs?

Balkanized federal controls over these dual-use substances exacerbate the problem, the report contends. Whereas the Centers for Disease Control and Prevention strictly monitors botulinum toxin used in research, that agency’s oversight ends once the toxin is in a pharmaceutical formulation. Then, the Food and Drug Administration only has to ensure the product’s safety for patients, not for the general public as potential terror targets.

The specter of global e-commerce in a bioweapon-turned-beauty-product is the latest reminder that the world has continued to change rapidly since 2001. In an age when FBI agents are using Twitter and Facebook to catch criminals, U.S. bioweapons policy needs to keep up with the times. Coleman and Zilinskas advocate a proactive

approach to the bogus Botox issue that could have wider applications. International collaborations between law enforcement and scientists to obtain counterfeit samples for molecular fingerprinting could help identify the illegal producers, who seem to be mainly in Asia and the former Soviet Union, and might allow the relevant governments to move in and shut them down. More innovative cooperation is needed now, before another biological weapons attack happens, to reduce the risk that it will.





# Millennium Development Goals at 10

A decade's worth of targeted accomplishments shows extreme poverty can be eliminated

BY JEFFREY D. SACHS



The eight Millennium Development Goals (MDGs) are in many ways the Cinderella of international development. When 160 world leaders met at the United Nations in September 2000, they were inspired to adopt the Millennium Declaration, including bold targets in the fight against

poverty, disease and hunger (learn more online at [www.un.org/millenniumgoals](http://www.un.org/millenniumgoals)). Such declarations are usually photo ops and little more. The MDGs, however, have become the belle of the ball. With an upcoming MDG Summit this September on their 10th anniversary, the MDGs can become the historic fulcrum for eliminating extreme poverty.

Two U.N. secretaries-general, Kofi Annan, who introduced the goals, and Ban Ki-moon, who energetically leads the fight for them today, have ensured that the goals embody the international commitment to banish life-and-death poverty. Global efforts are often weak and disorganized, but the MDGs are so straightforward, bold, practical and compelling—and with the legitimacy of universal endorsement by U.N. member states—that they have become the organizing principles of development programs in poor countries, assistance strategies of donor countries, and operational strategies of nongovernmental organizations (NGOs) around the world.

When Kofi Annan asked me in 2002 to direct the U.N. Millennium Project to identify feasible approaches to achieving the MDGs, I found that the world's scientific and practitioner communities, as well as many leading companies, were prepared to volunteer vast efforts for MDG success. We also learned, through a global network of hundreds of leading thinkers, practitioners and businesses, that the various goals—to reduce hunger, ensure school attendance, prevent childhood deaths, control pandemic diseases, fight gender bias, and more—could be spurred through very realistic investments and strategies.

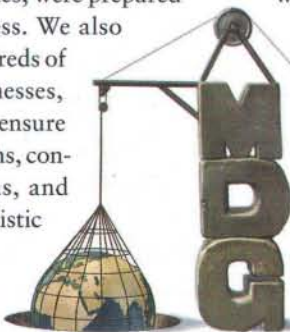
Ban Ki-moon's leadership on malaria control, part of the sixth MDG, exemplifies the point. In 2008 Ban called on the U.N. and its member states and on civil society to coalesce around a specific strategy to control malaria. The key is free access to long-lasting insecticide-treated nets to reduce malaria transmission, coupled with community-based drug treatments when episodes of malaria occur. With nearly 200 million bed nets distributed, malaria deaths are plummeting throughout Africa. The private-

sector bed net manufacturers have played a crucial role in ensuring a massive scale-up of coverage and access. Ban's Special Envoy for Malaria, Ray Chambers, reports that comprehensive bed net coverage is within reach by the end of 2010, as targeted.

President Barack Obama boldly pledged at the U.N. last September to come to this year's summit with "a global plan to make [the MDGs] a reality. And we will set our sights on the eradication of extreme poverty in our time." His administration's signature effort this year was the launch of a new global agriculture fund at the World Bank to finance increased production by smallholder farmers, thereby contributing to the first MDG, to slash hunger. As Malawi and other African countries have shown, targeted help for smallholder farmers can double food production within a year or two.

The model for malaria control, now being extended to smallholder farming, is powerful. Countries prepare national action plans, and if technical experts review and approve those plans, a global fund disburses money for bed nets, malaria medicines, high-yield seeds, fertilizer, and the like. These disbursements, being highly targeted and measurable, are easily monitored to verify efficacy and to avoid corruption. This approach can apply to a range of challenges: universal school attendance, access to community health workers and local health systems, the spread of rural electrification through solar and other renewable power, and the decisive reduction in women's deaths during childbirth. In this way, the defined targets of the MDGs come within quick reach.

Without question, the MDGs have spurred remarkable progress, but the challenges remain huge. Success will require plans at the September MDG Summit that concretely link governments, businesses, NGOs and individuals to clear national strategies. What might have been a mere get-together a decade ago to ring in the new millennium could yet prove to be the decisive organizing principle for ending extreme poverty in our time. ■



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An extended version of this essay is available at [www.ScientificAmerican.com/jun2010](http://www.ScientificAmerican.com/jun2010)



# When Ideas Have Sex

How free exchange between people increases prosperity and trust

BY MICHAEL SHERMER



In his 1776 work *An Inquiry into the Nature and Causes of the Wealth of Nations*, Scottish moral philosopher Adam Smith identified the cause in a single variable: “the propensity to truck, barter, and exchange one thing for another.”

Today we call this free trade or market capitalism, and since the recession it has become de rigueur to dis the system as corrupt, rotten or deeply flawed.

If we pull back and take a long-horizon perspective, however, the free exchange between people of goods, services and especially ideas leads to trust between strangers and prosperity for more people. Think of it as ideas having sex. That is what zoologist and science writer Matt Ridley calls it in his book *The Rational Optimist: How Prosperity Evolves* (HarperCollins, 2010). Ridley is optimistic that “the world will pull out of the current crisis because of the way that markets in goods, services and ideas allow human beings to exchange and specialize honestly for the betterment of all.”

Sex evolved because the benefit of the diversity created through the intermixture of genomes outweighed the costs of engaging in it, and so we enjoy exchanging our genes with one another, and life is all the richer for it. Likewise ideas. “Exchange is to cultural evolution as sex is to biological evolution,” Ridley writes, and “the more human beings diversified as consumers and specialized as producers, and the more they then exchanged, the better off they have been, are and will be. And the good news is that there is no inevitable end to this process. The more people are drawn into the global division of labour, the more people can specialize and exchange, the wealthier we will all be.”

In the teeth of the recession and the reality of more than a billion impoverished people in developing countries today, this thesis sounds ripe for skepticism, indeed almost blindly Pollyannish. But Ridley systematically builds a case through copious data and countless studies that “the vast majority of people are much better fed, much better sheltered, much better entertained, much better protected against disease and much more likely to live to old age than their ancestors have ever been. The availability of almost everything a person could want or need has been going

rapidly upwards for 200 years and erratically upwards for 10,000 years before that: years of lifespan, mouthfuls of clean water, lungfuls of clean air, hours of privacy, means of traveling faster than you can run, ways of communicating farther than you can shout,” and with more access to “calories, watts, lumen-hours, square feet, gigabytes, megahertz, light-years, nanometers, bushels per acre, miles per gallon, food miles, air miles, and of course dollars than any that went before.”

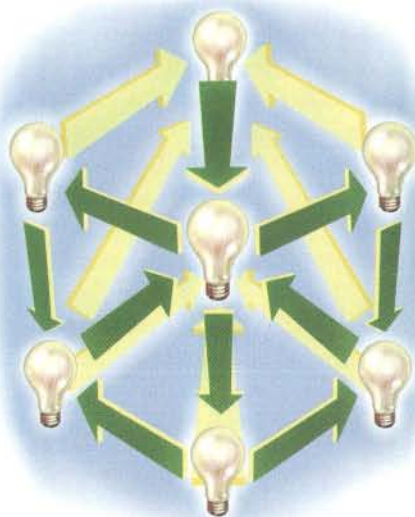
Trade does something even more important than enrich our lives. It makes people behave more fairly. In a March 18 article in *Science* entitled “Markets, Religion, Community Size, and the Evolution of Fairness and Punishment,” University of British Columbia psychologist Joseph Henrich and his

colleagues engaged nearly 2,700 people in 15 small communities around the world in two-player exchange games in which one subject is given a sum of money (the equivalent of a day’s pay) and allowed to keep or share some or all of it with another person. You would think that most people would just keep all of the money, but in fact the scientists discovered that members of hunter-gatherer communities shared about 25 percent, whereas members of societies who regularly engage in trade gave away about 50 percent. Although religion was a modest factor in making people more generous, the strongest predictor was “market integration,” defined as “the percentage of a household’s total calories that were purchased from the market, as opposed to homegrown, hunted, or fished.” Why? Because, the authors conclude, trust and cooperation with strangers lowers transaction costs and generates greater prosperity for all involved, and thus concepts of fair trade emerged as part of a larger process of social evolution to maintain mutually beneficial exchanges even when the participants were not bound by kinship, status or other social ties.

In other words, our ancestors had sex with people they knew, but their ideas had sex with strangers, and this form of trade led to trust and prosperity.

■

Michael Shermer is publisher of *Skeptic* magazine ([www.skeptic.com](http://www.skeptic.com)) and author of *The Mind of the Market*.





# Why I Love Neutrinos

The particles that once seemed impossibly esoteric have become ever more informative

BY LAWRENCE M. KRAUSS



**I'll admit it. I am partial to neutrinos. And I always have been.**

Neutrinos alone, among all the known particles, have ethereal properties that are striking and romantic enough both to have inspired a poem by John Updike and to have sent teams of scientists deep underground for 50 years to build huge science-fictionlike contraptions to unravel their mysteries.

It never ceases to amaze me that every second of every day, more than 6,000 billion neutrinos coming from nuclear reactions inside the sun whiz through my body, almost all of which will travel right through the earth without interruption. But I am even more amazed that in spite of their ghostliness, we can detect them, probe them and unravel their mysteries.

That is why, during the 30-odd years in which I have been a practicing physicist, my research has continually returned to these astonishing particles. And over the past months neutrinos have again reminded me in a very personal way of how daring science allows us to be in our imagination.

Emboldened by the remarkable experimental detection of solar neutrinos by the late Raymond Davis, Jr., 26 years ago, several colleagues and I started to think about other natural sources of neutrinos. One was right below our feet, literally. Radioactive elements sometimes produce antineutrinos (the antiparticles of neutrinos), and when we calculated how many such antineutrinos might be produced by all the radioactive materials thought to be in the earth, the number was almost as large as the solar neutrino flux across a small energy range. But as we tried to think of ways to detect these particles—which, as I began to learn a little geophysics, I recognized might reveal a lot about the makeup of the earth—we also realized that it would be much harder than it had been for Davis to detect solar neutrinos (which was plenty hard). So we wrote up the paper, figuring such a study would never be done.

But we also proposed an even more esoteric source. We knew that when stars explode as supernovae, 10,000 times more energy in the explosion should go into a stunning burst of neutrinos than into the emitted light. We also knew that astrophysical arguments suggested about one star would explode per galaxy every century. Although no one had ever measured a neutrino from

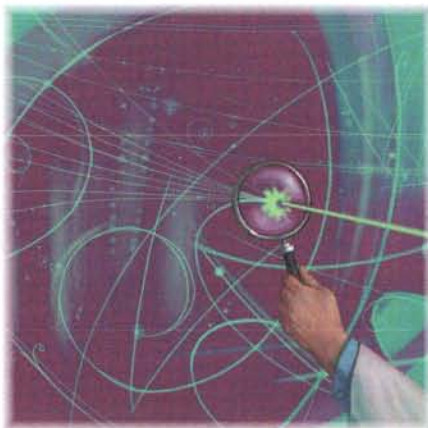
such an explosion, and there was no way at the time to get a direct observational handle on the very small presumed supernova rate in galaxies, we nonetheless decided to estimate what the flux of neutrinos on the earth should be from all stars that have exploded over cosmic history. I remember thinking at the time that it was surely the most impractical estimate I might ever make.

Flash forward to the present. This year the Borexino detector in Gran Sasso, Italy, a gargantuan liquid scintillation counter designed to catch solar neutrinos, reported an observation of “geoneutrinos” from the earth (with a less than one-in-10,000 chance of coming from other backgrounds), confirming an earlier, somewhat more tentative result from Japan. The observed rate is remarkably compatible with estimates from those indirect and theoretical geophysical arguments about the interior of the earth.

Meanwhile the Japanese instrument—the mammoth, 50,000-ton Super-Kamiokande (Super-K) water neutrino detector—has increased its sensitivity to be able to detect even a single supernova antineutrino-induced event per year, which is within striking distance of the rate from the cosmic background we had so casually estimated a generation ago. Remarkably, in the intervening time, however, neutrinos from a supernova explosion at the edge of our galaxy in 1987 were observed, and sophisticated imaging and data-analysis techniques now allow us to detect supernovae in distant galaxies, thereby refining our knowledge of their frequency. It turns out that the predicted rate at which Super-K should detect antineutrino events is strikingly consistent with our original guesstimate.

Once I was deeply skeptical that we would ever detect such things or that the faith in fundamental physics that heartened us to make speculations which seemed like science fiction would be so vindicated. It brings home the true power of science to probe hitherto unimaginable realms of the hidden universe all around us—a universe populated not by ghosts and spirits, but by objects far more interesting.

*Lawrence M. Krauss, a theoretical physicist and science commentator, is Foundation Professor and director of the Origins Initiative at Arizona State University ([www.krauss.faculty.asu.edu](http://www.krauss.faculty.asu.edu)).*





# 12 EVENTS

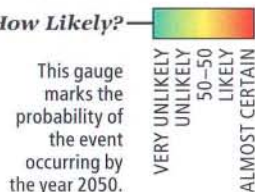
## that will change everything

### KEY CONCEPTS

- Several events, both natural and man-made, can happen suddenly and at any time, completely transforming societies.
- Many of these events will not unfold the way popular conceptions have imagined they will.

—The Editors

### How Likely?



The best science transforms our conception of the universe and our place in it and helps us to understand and cope with changes beyond our control. Relativity, natural selection, germ theory, heliocentrism and other explanations of natural phenomena have remade our intellectual and cultural landscapes. The same holds true for inventions as diverse as the Internet, formal logic, agriculture and the wheel.

What dramatic new events are in store for humanity? Here we contemplate 12 possibilities and rate their likelihood of happening by 2050. Some will no doubt bring to mind long-standing dystopian visions: extinction-causing asteroid collisions, war-waging intelligent machines, Frankenstein's monster. Yet the best thinking today suggests that many events will not unfold as expected. In fact, a scenario could be seen as sobering and disappointing to one person and curious and uplifting to another. One thing is certain: they all have the power to forever reshape how we think about ourselves and how we live our lives.

—The Editors

PHOTOGRAPHS BY KEVIN VAN AELST

## cloning of a human LIKELY

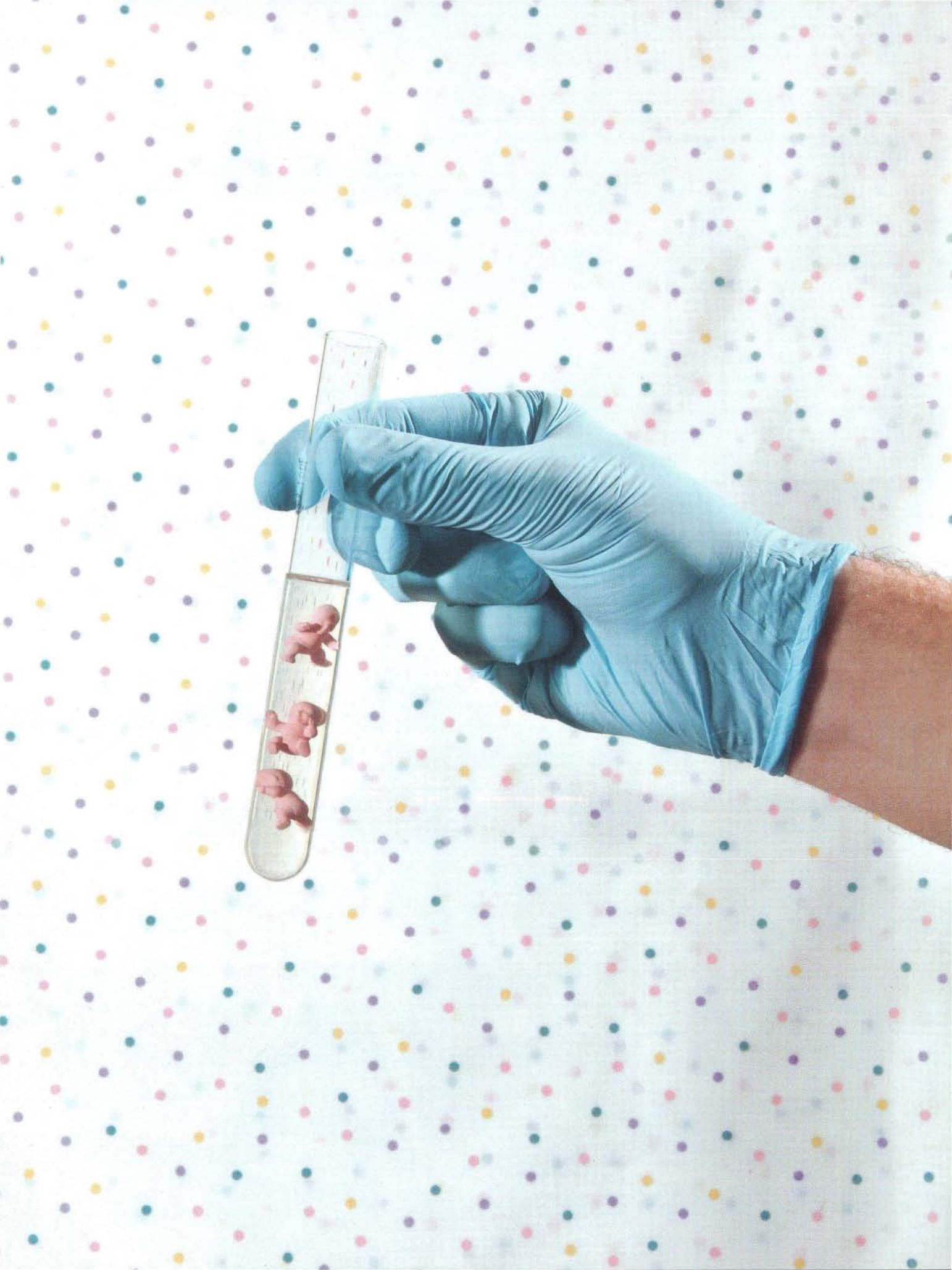
The process is extremely difficult, but it also seems inevitable *By Charles Q. Choi*

Ever since the birth of Dolly the sheep in 1996, human cloning for reproductive purposes has seemed inevitable. Notwithstanding past dubious claims of such an achievement—including one by a company backed by a UFO cult—no human clones have been made, other than those born naturally as identical twins. Despite

success with other mammals, the process has proved much more difficult in humans—which may strike some people as comforting and others as disappointing.

Scientists generate clones by replacing the nucleus of an egg cell with that from another individual. They have cloned human embryos, but none







has yet successfully grown past the early stage where they are solid balls of cells known as morulas—the act of transferring the nucleus may disrupt the ability of chromosomes to align properly during cell division. “Whenever you clone a new species, there’s a learning curve, and with humans it’s a serious challenge getting enough good-quality egg cells to learn with,” says Robert Lanza of Advanced Cell Technology in Worcester, Mass., who made headlines in 2001 for first cloning human embryos. Especially tricky steps include discovering the correct timing and mix of chemicals to properly reprogram the cell.

Even with practiced efforts, some 25 percent of cloned animals have overt problems, Lanza notes—minor slips during reprogramming, culturing or handling of the embryos can lead to developmental errors. Attempting to clone a human

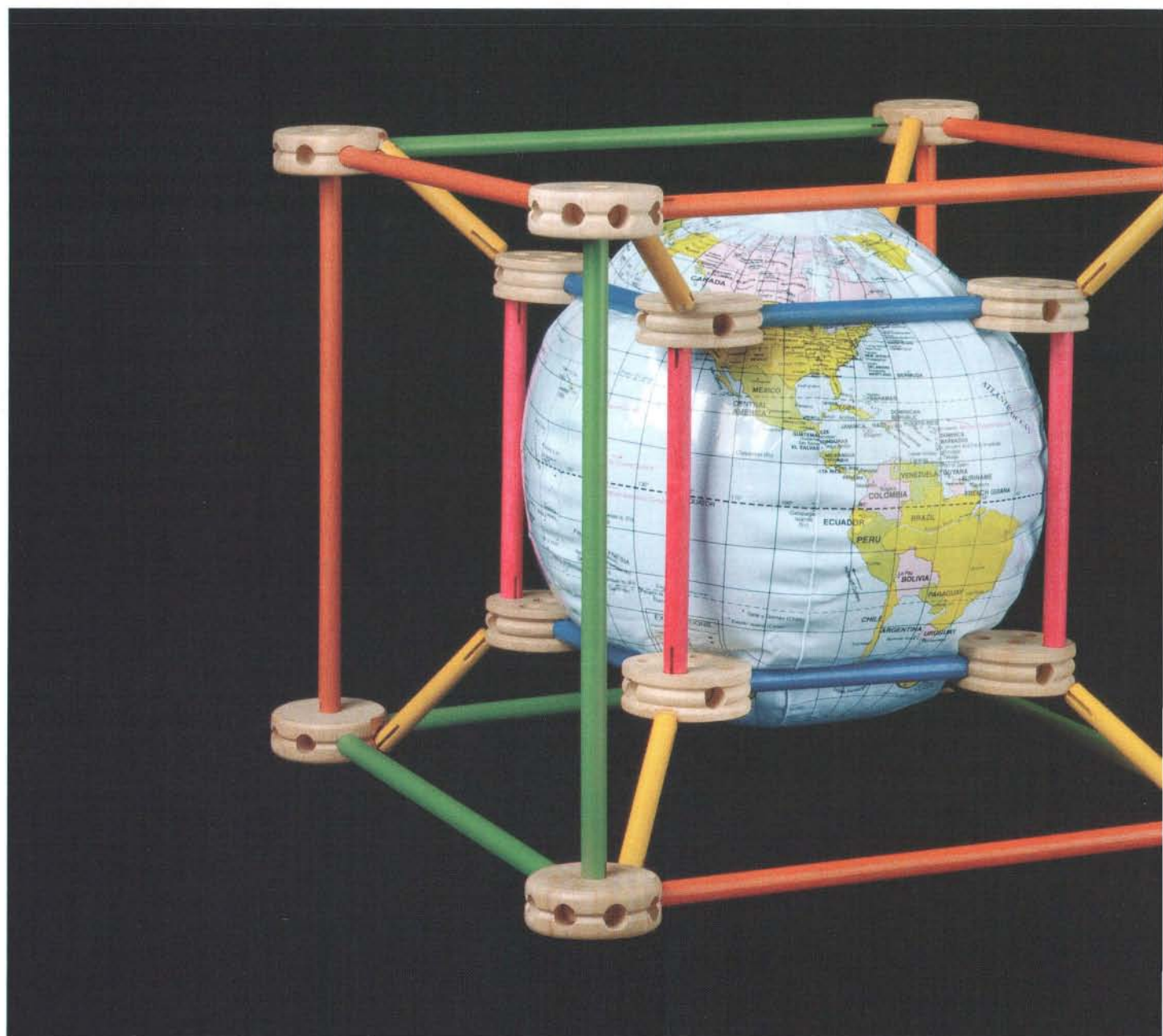
would be so risky, Lanza says, it “would be like sending a baby up into space in a rocket that has a 50–50 chance of blowing up.”

Ethical issues would persist even assuming foolproof techniques. For instance, could people be cloned without their knowledge or consent? On the other hand, a clone might lead a fuller life, because it “really gets to learn” from the original, says molecular technologist George M. Church of Harvard Medical School. “Say, if I learned at 25 I had a terrific ear for music but never got music lessons, I could tell my twin to try it at 5.”

The possibility of human cloning may not be restricted to *Homo sapiens*, either. Scientists may soon completely sequence the Neandertal genome. Although DNA is damaged during fossilization, an excellent fossil could yield enough molecules to generate a cloneable genome, Church

suggests. Bringing a cloned extinct species to term in a modern species is even more challenging than normal cloning, considering that such factors as the womb environment and gestation period might be mismatched. The only clone so far of an extinct animal—the bucardo, a variety of ibex that died off in 2000—expired immediately after birth because of lung defects.

In the U.S., not all states have banned human reproductive cloning. The United Nations has adopted a nonbinding ban. If human cloning happens, it will “occur in a less restrictive area of the world—probably by some wealthy eccentric individual,” Lanza conjectures. Will we recoil in horror or grow to accept cloning as we have in vitro fertilization? Certainly developing new ways to create life will force us to think about the responsibilities of wielding such immense scientific power.







## The world's biggest particle collider might uncover new slices of space *By George Musser*

**W**ouldn't it be great to reach your arm into a fourth dimension of space? You could then liberate yourself from the shackles of ordinary geometry. Hopelessly tangled extension cords would slip apart with ease. A left-handed glove could be flipped over to replace the right-handed one your dog ate. Dentists could do root canals without drilling or even asking you to open your mouth.

As fantastic as extra dimensions of space sound, they might really exist. From the relative weakness of gravity to the deep affinity among seemingly distinct particles and forces, various mysteries of the world around us give the impression that the known universe is but the shadow of a higher-dimensional reality. If so, the Large Hadron Collider (LHC) near Geneva could smash particles together and release enough energy to break the shackles that keep particles in three dimensions and let us reach into that mind-blowing realm.

Proof of extra dimensions "would alter our whole notion of what reality is," says cosmologist Max Tegmark of the Massachusetts Institute of Technology, who in 1990 wrote a four-dimensional version of the video game Tetris to get a taste of what extra dimensions might be like. (You keep track of the falling blocks using multiple 3-D slices of the full 4-D space.)

In modern physics theories, the main rationale for extra dimensions is the concept of supersymmetry, which aims to unite all the different types of particles into one big happy family. Supersymmetry can fulfill that promise only if space has a total of 10 dimensions. The dimensions could have gone unnoticed either because they are too small to enter or because we are, by our very nature, stuck to a 3-D membrane like a caterpillar clutching onto a leaf.

To be sure, not every proposed unified theory involves extra dimensions. So their discovery or nondiscovery would be a helpful data point. "It would focus what we do," says physicist Lisa Randall of Harvard University, who made her name studying the caterpillar-and-leaf option.

One way to get at those dimensions is to crank up the energy of a particle accelerator. By the laws of quantum mechanics, the more energy a particle has, the more tightly confined it is; an energy of one tera-electron-volt (TeV) corresponds to a size of  $10^{-19}$  meter. If an extra dimension is that big, the particle would

literally fall into it and begin to vibrate.

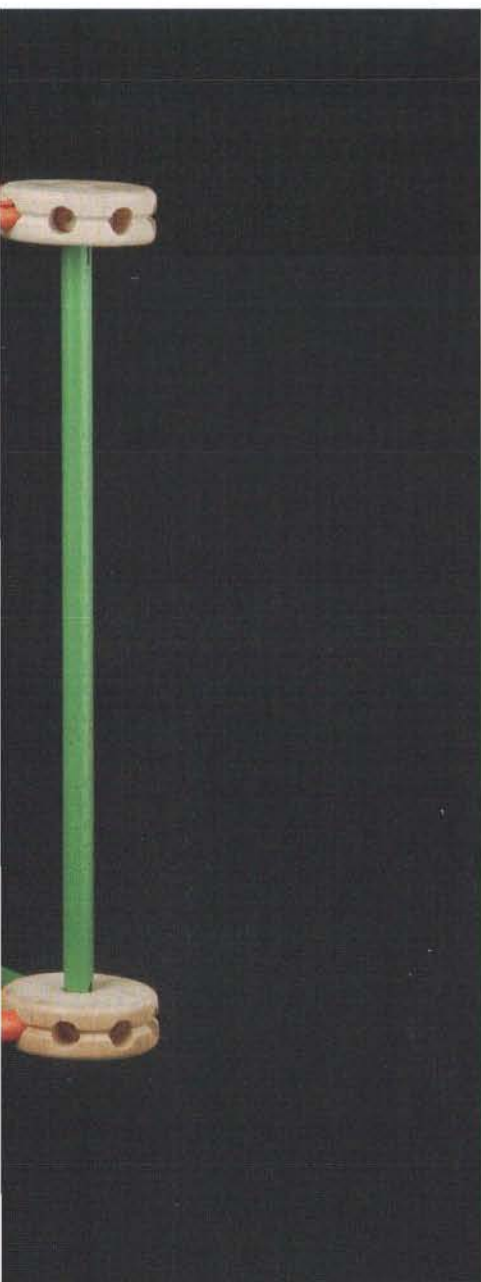
In 1998 physicist Gordon Kane of the University of Michigan at Ann Arbor imagined that the LHC smashed together two protons and created electrons and other particles that not only had the energy of 1 TeV but also integer multiples thereof, such as 2 or 3 TeV. Such multiples would represent the harmonics of the vibrations in extra dimensions set off by the collision. Neither standard particle processes nor exotica such as dark matter particles could account for these events.

Extra dimensions might betray themselves in other ways. If the LHC produced subatomic black holes, they would be immediate proof of extra dimensions, because gravity in ordinary 3-D space is simply too weak to create holes of this size. For geometric reasons, higher dimensions would strengthen gravity on small scales. They would likewise change the small-scale behavior of other forces, such as electromagnetism. And by dictating how supersymmetry operates, they might lead to distinctive patterns among the masses and other properties of particles. Besides the LHC, scientists might find hints of extra dimensions in measurements of the strength of gravity and in observations of the orbits of black holes or of exploding stars.

The discovery would transform not only physics but also its allied disciplines. Extra dimensions might explain mysteries such as cosmic acceleration and might even be a prelude to reworking the entire notion of dimensionality—adding to a growing sense that space and time emerge from physical principles that play out in a spaceless, timeless realm.

"So while extra dimensions would be a terrific discovery," says physicist Nima Arkani-Hamed of the Institute for Advanced Study in Princeton, N.J., "at a deeper level, conceptually they aren't particularly fundamental."

Whatever the charms of extra dimensions for physicists, we will never be able to visit them for ourselves. If they were open to the particles that make up our bodies, the added liberty of motion would destabilize complex structures, including life. Alas, the frustration of tangled cords and the pain of dental work are necessary trade-offs to allow us to exist at all.





UNLIKELY



# extraterrestrial intelligence

How will we respond to a signal from outer space? *By John Matson*

**F**ifty years ago a young astronomer, indulging in a bit of interstellar voyeurism, turned a telescope on the neighbors to see what he could see. In April 1960 at the National Radio Astronomy Observatory in Green Bank, W.Va., Frank Drake, then 29, trained a 26-meter-wide radio telescope on two nearby stars to seek out transmissions from civilizations possibly in residence there. The search came up empty, but Drake's Project Ozma began in earnest the ongoing search for extraterrestrial intelligence, or SETI.

Drake, who turned 80 in May, is still at it, directing the Carl Sagan Center for the Study of Life in the Universe at the nonprofit SETI Institute in Mountain View, Calif. Instead of just borrowing time from other astronomical instruments, those in the field now have purpose-built tools at their disposal, such as the fledgling Allen Telescope Array (ATA) in Hat Creek, Calif. But funding is scarce—the ATA growth stalled at 42 dishes of a planned 350—and astronomers have not yet gathered enough

data to make firm pronouncements about intelligent life in the universe.

"Although we have 'been doing it' for 50 years, we have not been on a telescope very much of that time," says Jill Tarter, director of the Center for SETI Research at the SETI Institute. "What we can say is that every star system in the galaxy isn't populated by a technology that's broadcasting radio signals at this time."

Theoretical astrophysicist Alan P. Boss of the Carnegie Institution for Science agrees. "The lack of a SETI signal to date simply means that civilizations that feel like broadcasting to us are not so common that the limited SETI searches would have found one," Boss says. "There is still a lot of the galaxy that has not yet been searched." One of the most extensive campaigns to date, Project Phoenix, surveyed nearby stars across a wide range of frequencies using some of the world's largest radio telescopes. In nine years Phoenix sampled roughly 800 stars, less than one millionth of 1 percent of the Milky Way.

Even for stars that have been scanned, the parameters for a possible signal are frustratingly numerous. Like those for terrestrial radio, they include frequency (what station does it broadcast on?), time (24/7 or midnight sign-off?), type of modulation (AM or FM?), and so on. "At the very least this search is nine-dimensional," Tarter says, "and we could guess right about what to look for and build the right instrument for eight of those dimensions, but we could still miss it because we got one wrong."

Arguments for SETI and for widespread life in general have been bolstered by the confirmation that planetary systems are common around other stars. Most of the 400-plus exoplanets are scalding giants inhospitable to life as we know it. But in the next few years NASA's Kepler space telescope, now surveying more than 100,000 stars for planets, should settle the question of how common Earth-like planets are.

Even on Earth-like worlds, however, technological, radio-broadcasting life may not be common. Many researchers hold out more hope for finding simpler life-forms, such as microbes or slime molds. Boss says that life of this kind should be widespread, but we will not have the technology to detect it for two decades at best.

But what if someone does pick up a signal from an intelligent civilization? The SETI community has protocols in place, such as alerting observatories around the world for verification, but the same cannot be said of the world's governments. A United Nations-level framework does not yet exist to guide the contentious next steps—if we hear a shout from a potentially hostile neighbor, do we dare shout back?

It would not be an entirely new experience for Drake, who as a graduate student thought he had made a detection. "You feel a very special emotion if you think that has happened, because you realize everything is going to change," he says, noting that we would soon be enriched with new knowledge of other worlds, species and cultures. "It's an emotion you have to feel to understand, and I felt it."

UNLIKELY



# nuclear exchange

A local conflict could produce a global nightmare *By Philip Yam*

**T**he end of the cold war and ongoing arms-control efforts by the U.S., Russia and other countries have greatly reduced the threat of global nuclear annihilation. But rogue nations and continued tensions make a local exchange of nuclear firepower all too real.

A single detonation can cause horrible death in several ways. The Hiroshima blast—equal to about 15 kilotons of TNT—generated supersonic wind speeds that crushed concrete buildings near ground zero. Heat from the blast scorched to death anyone within one kilometer. People many kilometers away eventually succumbed to radiation poisoning and cancer.

Global effects, however, would not happen unless dozens of bombs exploded, as might occur in an exchange between Pakistan and India. In modeling the effects, scientists have assumed that those nations would unload their entire ar-

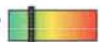
senals, so that about 100 Hiroshima-size bombs would go off [see "Local Nuclear War, Global Suffering," by Alan Robock and Owen Brian Toon; *SCIENTIFIC AMERICAN*, January].

Aside from 20 million killed in the war, many outside the conflict would perish over time. That is because the blasts would throw up five million metric tons of soot into the upper atmosphere. Driven by weather patterns, the particulates would encircle the globe in about a week; within two months they would blanket the planet. Darkened skies would rob plants of sunlight and disrupt the food chain for 10 years. The resulting famine could kill the one billion people who now survive on marginal food supplies.

The outcome is grim. But there is one bright spot: it is within humanity's ability—and responsibility—to see that such a world-changing event never happens.



UNLIKELY



## asteroid collision

An extinction-level event is unlikely, but "airbursts" could flatten a city *By Robin Lloyd*

**O**n June 13 an asteroid called 2007 XB10 with a diameter of 1.1 kilometers—and the potential to cause major global damage—will zip past Earth. As far as near-Earth objects go, it will pass, fortunately, pretty far, at 10.6 million kilometers, or 27.6 times the Earth-moon distance. Indeed, no giant asteroids appear poised to rewrite history any time soon. The bad news is that we can expect in the next 200 years a small space rock to burst in the atmosphere with enough force to devastate a small city.

A near-Earth object (NEO) is an asteroid or comet that comes within 195 million kilometers of the planet. In 2009 NASA tallied 90 as approaching within five lunar distances and 21 within one lunar distance or less. NEO hunters typically detect them as specks on images, and such momentary glimpses can make their orbits hard to calculate. So researchers can

only lay odds of an impact as they await more data. NASA has spotted 940 NEOs one kilometer or more in diameter (about 85 percent of the estimated total of that size), and none will collide with Earth. (The NEO that wiped out the dinosaurs was about 10 kilometers wide.)

The bigger threat now, however, involves the smaller rocks, according to a National Research Council (NRC) report released earlier this year. These asteroids and comets—100,000 or so of them span 140 meters or more—are too small to bring about an Armageddon, but even those at the lowest end of that range could deliver an impact energy of 300 megatons of TNT. And these events occur on average far more frequently (every 30,000 years or so for a 140-meter object) than, say, a one-kilometer impact (every 700,000 years).

Given the possible danger, Congress mandated in 2005 that NASA find 90 per-

cent of such NEOs by 2020. But budget shortfalls will make it impossible for scientists to meet that deadline, the NRC has found. NEO hunters get about \$4 million in federal funding annually.

In any case, in terms of risk, researchers are thinking even smaller, because the most likely NEO scenario is a 30- to 50-meter-diameter "city killer," a bolide that would detonate in the atmosphere. The most famous of such devastating "airbursts" occurred in 1908 over Tunguska, Siberia, an event that flattened an area the size of London. The famous Meteor Crater in Barringer, Ariz., resulted from a meteorite in this size category.

At this point, some of the best information on airbursts is kept by the U.S. Department of Defense, Department of Energy and Comprehensive Test Ban Treaty monitoring stations. The NRC report, which asks for more sharing of these closely held data, estimates that 25-meter airbursts occur every 200 years. Most explode over the oceans where the direct risk to life is low but where the initiation of a tsunami is possible. Panel member Mark Boslough of Sandia National Laboratories says a four-meter object blazes in once every year.

And what would we do if we spot a NEO with our name on it? Realistic mitigation plans are in their infancy, says NRC panelist Michael F. A'Hearn of the University of Maryland. For moderately big objects and with notice of years or decades, kinetic impactors make the most sense. The idea is to slam one or more large spacecraft into an object to alter its path. Nuclear detonation is the only option for NEOs exceeding 500 meters across when warning time is months to years.

For city-destroying sizes and short lead times, the choices are limited, perhaps restricted only to evacuation, which we would be lucky to pull off effectively at this point, A'Hearn thinks. All the more reason, it seems, to be thankful that nothing's headed our way—as far as we know.

50-50



## deadly pandemic

Notwithstanding the tameness of H1N1, influenza viruses could still wipe out millions and wreak economic havoc *By Katherine Harmon*

**T**he H1N1 virus has packed less of a pandemic punch than initially feared, but it has uncovered some hard truths about our readiness—or lack thereof—for coping with a more deadly pathogen. Despite vast medical advances since the 1918 influenza epidemic, a novel, highly contagious illness could still devastate populations and upend social, economic, political and legal structures the globe over.

A new virulent strain—of flu or any other virus—could kill off millions, even those who appear to be in their prime, says Lawrence O. Gostin, a professor of global health law at Georgetown University. In addition, many nations would likely close borders, an action that would be accompanied by discrimination against individuals and recrimination among governments. International trade and commerce would drop, which would have "enormous financial

implications," says Gostin, who estimates a 3 to 5 percent drop in global GDP (amounting to a loss of \$1.8 trillion to \$3 trillion). This cycle of instability and contagion could last "on the order of years," he notes, as subsequent waves of an illness arrive with changing seasons.

In situations where a viral threat is just becoming apparent, policy makers and others would have to make tough decisions with imperfect and incomplete information. Basic human rights could face challenges as governments tried to subdue the spread.

If the contagious affliction came from a human malefactor, the social upheaval would most likely be worse. "The burden of morbidity and mortality would be lower," Gostin remarks, but "when it's man-made, people fear the worst. It's very socially and economically disruptive—more so than a natural disaster."

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## Synthetic biology remakes organisms, but can it bring inanimate matter to life? *By David Biello*

A scientist adds a few chemical compounds to a bubbling beaker and gives it a swirl. Subtle reactions occur, and, lo and behold, a new life-form assembles itself, ready to go forth and prosper. Such is the popular imagining of synthetic biology, or life created in the lab.

But researchers in this field are not as interested in animating the inanimate. In fact, scientists remain far from understanding the basic processes that could allow inert, undirected compounds to assemble into living, self-replicating cells. The famous Miller-Urey experiment of 1952, which created amino acids from primordial goo, remains difficult to replicate conclusively.

Rather synthetic biology today is about modifying existing organisms. It can be seen as genetic engineering on steroids: instead of replacing one gene, synthetic biologists modify large chunks of genes or even entire genomes. The change in DNA can force organisms to churn out chemicals, fuels and even medicines. "What they're doing is constructing from scratch the instruction set for life and adding that to something already alive, replacing the natural instruction set," explains biological engineer Drew Endy of Stanford University. "It defines an alternative path forward for promulgating life on earth. You no longer need to descend directly from a parent."

In that regard, some scientists do not see any reason to replicate an existing cell with a man-made one. "Making something as close as possible to an existing cell, you might as well use the existing cell," argues geneticist and technology developer George M. Church of Harvard Medical School. And manipulating genomes has become so widespread that even high schoolers do it.

Synthetic biology, in fact, is all about bringing the principles of large-scale engineering to biology. Imagine a world where bamboo is programmed to grow into a chair, rather than roughly woven into that shape through mechanical or human in-

dustry, or where self-assembling solar panels (otherwise known as leaves) feed electricity to houses. Or trees that exude diesel fuel from their stems. Or biological systems that are reengineered to remove pollution or to thrive in a changing climate. Reprogrammed bacteria might even be able to invade our bodies to heal, acting as an army of living doctors inside us.

"In principle, everything that is manufactured could be manufactured with biology," Church argues. It is already happening on a small scale: enzymes from high-temperature microbes used in laundry detergent have been reengineered to perform in cold water, thereby saving energy.

Synthetic biology "is going to fundamentally change the way we make everything for the next 100 years," predicts David Rejeski, director of the science, technology and innovation program at the Woodrow Wilson International Center for Scholars in Washington, D.C. "We can engineer matter at a biologically relevant scale. That's as big a change as the industrial revolution back in the 19th century."

With great promise comes great risk, too—namely, in the form of modified organisms escaping the lab. Most such creations today are too ungainly to survive in the wild. For more sophisticated creations in the future, synthetic biologists expect that various safeguards would need to be instituted, such as strict monitoring or a kind of self-destruct sequence in the new genetic code. Because scientists can entirely remake organisms at the genetic level, they can insulate them from natural systems, Endy says: "We can make them fail fast."

Nevertheless, some scientists are indeed attempting to re-create life. Carole Lartigue, Hamilton Smith and others at the J. Craig Venter Institute have made a bacterial genome from scratch and even turned one type of microbe into another. Researchers elsewhere have created synthetic organelles and even an entirely novel organelle, the so-called synthosome, to make

enzymes for synthetic biology. Life from scratch may be imminent.

Such a feat does not mean scientists will understand how life arose in the first place, but it might provoke fears that humanity has achieved the undesired power of deities. But the creation could also have a more humbling effect—by transforming our understanding of our fellow life-forms. "The benefits would be to remake our civilization in partnership with life at the molecular level to sustainably produce the materials, energy and feedstocks we need," Endy says. "We will have a balance of partnership with the rest of life on the planet in a way that is very different from the way we now interact with nature."







## room-temperature superconductors 50-50

They would transform the grid—if they can exist at all *By Michael Moyer*

**Y**ou can build a coal-fired power plant just about anywhere. Renewables, on the other hand, are finicky. The strongest winds blow across the high plains. The sun shines brightest on the desert. Transporting that energy into cities hundreds of kilometers away will be one of the great challenges of the switch to renewable energy.

The most advanced superconducting cable can move those megawatts thousands of kilometers with losses of only a few percent. Yet there is a catch: the cable must be kept in a bath of liquid nitrogen at 77 kelvins (or  $-196$  degrees Celsius). This kind of deployment, in turn, requires pumps

and refrigeration units every kilometer or so, greatly increasing the cost and complexity of superconducting cable projects.

Superconductors that work at ordinary temperatures and pressures would enable a truly global energy supply. The Saharan sun could power western Europe via superconducting cables strung across the floor of the Mediterranean Sea. Yet the trick to making a room-temperature superconductor is just as much of a mystery today as it was in 1986, when researchers constructed the first superconducting materials that worked at the relatively high temperatures of liquid nitrogen (previ-

ous substances needed to be chilled down to 23 kelvins or less).

Two years ago the discovery of an entirely new class of superconductor—one based on iron—raised hopes that theorists might be able to divine the mechanism at work in high-temperature superconductors [see “An Iron Key to High-Temperature Superconductivity?” by Graham P. Collins; *SCIENTIFIC AMERICAN*, August 2009]. With such insights in hand, perhaps a path toward room-temperature superconductors would come into view. But progress has remained slow. The winds of change don’t always blow on cue.



LIKELY

# machine self-awareness

What happens when robots start calling the shots? *By Larry Greenemeier*

Artificial-intelligence (AI) researchers have no doubt that the development of highly intelligent computers and robots that can self-replicate, teach themselves and adapt to different conditions will change the world. Exactly when it will happen, how far it will go, and what we should do about it, however, are cause for debate.

Today's intelligent machines are for the most part designed to perform specific tasks under known conditions. Tomorrow's machines, though, could have more autonomy. "As the kinds of tasks that we want machines to perform become more complex, the more we need them to take care of

themselves," says Hod Lipson, a mechanical and computer engineer at Cornell University. The less we can foresee issues, Lipson points out, the more we will need machines to adapt and make decisions on their own. As machines get better at learning how to learn, he says, "I think that leads down the path to consciousness and self-awareness."

Although neuroscientists debate the biological basis for consciousness, complexity seems to be a key part, suggesting that computers with adaptable and advanced hardware and software might someday become self-aware. One way we will know that machines have attained that cognitive

level is that they suddenly wage war on us, if films such as *The Terminator* are correct. More likely, experts think, we will see it coming.

That conceit derives from observations of humans. We are unique for having a level of intelligence that enables us to repeatedly "bootstrap" ourselves up to reach ever greater heights, says Selmer Bringsjord, a logician and philosopher at Rensselaer Polytechnic Institute. Whereas animals seem to be locked into an "eternally fixed cognitive prison," he says, people have the ability to free themselves from their cognitive limitations.

Once a machine can understand its own exis-





tence and construction, it can design an improvement for itself. "That's going to be a really slippery slope," says Will Wright, creator of the Sims games and co-founder of Berkeley, Calif.-based robotics workshop the Stupid Fun Club. When machine self-awareness first occurs, it will be followed by self-improvement, which is a "critical measurement of when things get interesting," he adds. Improvements would be made in subsequent generations, which, for machines can pass in only a few hours.

In other words, Wright notes, self-awareness leads to self-replication leads to better machines made without humans involved. "Personally, I've always been more scared of this scenario than a lot of others" in regard to the fate of humanity, he says. "This could happen in our lifetime. And once we're sharing the planet with some form of super-intelligence, all bets are off."

Not everyone is so pessimistic. After all, machines follow the logic of their programming, and if this programming is done properly, Bringsjord says, "the machine isn't going to get some supernatural power." One area of concern, he notes, would be the introduction of enhanced machine intelligence to a weapon or fighting machine behind the scenes, where no one can keep tabs on it. Other than that, "I would say we could control the future" by responsible uses of AI, Bringsjord says.

This emergence of more intelligent AI won't come on "like an alien invasion of machines to replace us," agrees futurist and prominent author Ray Kurzweil. Machines, he says, will follow a path that mirrors the evolution of humans. Ultimately, however, self-aware, self-improving machines will evolve beyond humans' ability to control or even understand them, he adds.

The legal implications of machines that operate outside of humanity's control are unclear, so "it's probably a good idea to think about these things," Lipson says. Ethical rules such as the late Isaac Asimov's "three laws of robotics"—which, essentially, hold that a robot may not injure a human or allow a human to be injured—become difficult to obey once robots begin programming one another, removing human input. Asimov's laws "assume that you program the robot," Lipson says.

Others, however, wonder if people should even govern this new breed of AI. "Who says that evolution isn't supposed to go this way?" Wright asks. "Should the dinosaurs have legislated that the mammals not grow bigger and take over more of the planet?" If control turns out to be impossible, let's hope we can peaceably share the planet with our silicon-based companions.

## polar meltdown LIKELY

Move the beach chair back: rising seas will literally reshape the world *By David Biello*

**T**he U.S. is shrinking—physically. It has lost nearly 20 meters of beach from its East Coast during the 20th century. The oceans have risen by roughly 17 centimeters since 1900 through expansion (warmer water taking up more space) and the ongoing meltdown of polar ice.

That increase, however, is a small fraction compared with what's to come. "Plan for one meter by the end of this century," says glaciologist Robert Bindshadler, an emeritus scientist at NASA. "The heat in the ocean is killing the ice sheet."

Some of the famous predictions—Florida under five meters of sea-level rise and a gaping bay where Bangladesh used to be—may be centuries away. But expect an ice-free Arctic and different coastal contours by 2100. By the reckoning of economist Nicholas Stern of the London School of Economics, 200 million people live within one meter above the present sea level, including eight out of 10 of the world's largest cities and all the megacities of the developing world. "They're going to have to move," Bindshadler suggests.

In fact, unless greenhouse gas emissions are tamed, the seas will keep rising as the ice sheets covering mountain ranges

(constituting roughly 1 percent of the planet's ice), Greenland (9 percent) and Antarctica (90 percent) melt away. All told, they harbor enough water to eventually raise sea levels by at least 65 meters.

It takes centuries to melt an entire ice sheet, but still, the ice is disappearing faster than scientists had expected even a few years ago. Even with gradual sea-level rise, the risk of catastrophic storm surges and the like creeps up.

The gravitational pull of ice on surrounding waters is a recently appreciated surprise, too: generally speaking, if Greenland ice melts, "most of the sea-level rise occurs in the Southern Hemisphere," and vice versa for Antarctic ice, says physicist W. Richard Peltier of the University of Toronto. "West Antarctica is the region we believe is most susceptible to destabilization by ongoing global warming."

Even if greenhouse gas emissions decline, the polar meltdowns will be difficult to avoid because ice sheets lag the overall climate and, once melted, have a hard time re-forming. Just how humans will adapt to a more watery world is still not known. Of today's trend, Bindshadler notes, "We're not going to avoid this one."



ALMOST CERTAIN



## pacific earthquake

Will the overdue Big One tear California asunder? *By Katherine Harmon*

**L**os Angeles might not end up as an island when the Big One rocks California, but any sizable seismic event on the San Andreas fault will send L.A. several meters closer to San Francisco. Scientists and the public have long expected a major quake to strike the West Coast; the U.S. Geological Survey estimates that California has a 99 percent chance before 2038 of experiencing at least a magnitude 6.7 quake—the same size as the 1994 Northridge earthquake.

But it could easily be bigger. Much bigger. If most of the San Andreas were to rupture in one event, an earthquake could reach a magnitude 8.2, says Lucy Jones, chief scientist of the Multi-Hazards Demonstration Project at the USGS in southern California.

The San Andreas fault runs about 1,300 kilometers from southern California up past the Bay Area. It forms the boundary between the North American plate, moving southeasterly, and the Pacific plate,

heading to the northwest. From geologic records, scientists think that the fault usually ruptures about once every 150 years. The last big movement, however, was about 300 years ago.

A magnitude 7.8 earthquake (which a 2008 USGS and California Geological Society report calls a “plausible event”) would shake some 10 million southern Californians, killing about 1,800 and injuring 50,000. A rumble this size, which the USGS modeled as the ShakeOut Earthquake





Scenario outreach project, would mean a fault movement of about 13 meters. Such a slip would sever roads, pipelines, railways and communications cables that cross the fault and trigger landslides. Aftershocks—some as powerful as magnitude 7.2—would rattle the region for weeks. The quake would cause some \$200 billion in damage, and long-term infrastructure and business disruption would cost billions more, Jones notes.

But the San Andreas isn't the only fault likely to slip, and seismic activity along one fault—even one thousands of kilometers away—can set off others that are getting ready to go. An offshore 6.5 quake that shook northern California in January oc-

curred on the southern edge of the Cascadia subduction zone, which runs just offshore of the Pacific Northwest. This plate boundary could unleash at least a magnitude 9.0—the size of the 2004 Sumatra quake that spawned a devastating tsunami. Geologic records show evidence of an earthquake in 1700 that sent a tsunami all the way to Japan, and a similarly sized quake has about a one-in-10 chance of occurring in the next few decades.

Predicting earthquakes is a little bit like trying to guess your weather for the week based on knowing the climate, says geophysicist Robert Yeats of Oregon State University. Realizing that a quake will probably occur sometime soon, he adds, “doesn’t affect your holiday plans, but it’s going to affect your building codes.” The bigger buildings can be among the safest—some of the state’s skyscrapers having been built to

withstand magnitudes upward of 7.8. And just because a big earthquake appears overdue, the next seismic shift might not lead to the worst-case scenario. Scientists are still learning more about the frequency of big quakes (greater than magnitude 6.0) in the geologic record, and some newer evidence suggests that smaller earthquakes might be more the norm on the San Andreas.

When the Big One does come, it might not prove as devastating as long feared thanks to modern, savvy construction and public readiness campaigns. Much greater havoc can come from even moderate earthquakes in poorer, less prepared areas of the world. The January quake in Haiti, for instance, killed nearly a quarter of a million people—a sobering example of how a sudden slip of a fault can quickly crumble cities that have not had the luxury of careful planning.

## fusion energy

VERY UNLIKELY

It would solve environmental headaches, but it remains hard to achieve *By Michael Moyer*

**A**ccording to the old quip, a practical fusion reactor will always be about 20 years away. Nowadays that feels a bit optimistic. The world’s largest plasma fusion research project, the ITER reactor in southern France, won’t begin fusion experiments until 2026 at the earliest. Engineers will need to run tests on ITER for at least a decade before they will be ready to design the follow-up to that project—an experimental prototype that could extract usable energy from the fusing plasma trapped in a magnetic bottle. Yet another generation would pass before scientists could begin to build reactors that send energy to the grid.

And meanwhile there is no end to world’s energy appetite. “The need for energy is so great and growing so rapidly around the world that there has to be a new approach,” says Edward Moses, director of the National Ignition Facility, a major fusion test facility in Livermore, Calif., that focuses laser beams onto a small fuel pellet to induce fusion.

In theory, fusion-based power plants would provide the answer. They would be fueled by a form of heavy hydrogen found in ordinary seawater and would produce no harmful emissions—no sooty pollutants, no nuclear waste and no greenhouse gases. They would harness the forces at work inside the sun to power the planet.

In practice, however, fusion will probably not change the world as physicists have imagined. The technology needed to trigger and control self-sustaining fusion has proved elusive. Moreover, the first reactors will almost certainly be too expensive to deploy widely this century.

Moses and others believe that the fastest route to harness fusion energy is to use a hybrid approach, employing fusion reactions to accelerate fission reactions in nuclear waste. In this method, called LIFE (for laser inertial fusion engine), powerful lasers focus their energy onto a small fuel pellet. The blasts ignite brief bursts of fusion. The neutrons from these fusion reactions travel outward and strike a shell of fissile material—either the spent fuel from an ordinary nuclear power plant or depleted uranium, a common ordnance. When the neutrons strike the radioactive waste, they trigger additional decays that generate heat for energy production and accelerate the breakdown of the material into stable products (thus solving the nuclear waste disposal problem as well). Moses claims he could build an engineering prototype of the LIFE design by 2020 and connect a working power plant to the grid by 2030.

In other words, a practical fusion reactor is only about 20 years away.







# Alzheimer's: Forestalling the Darkness

In his magical-realist masterpiece *One Hundred Years of Solitude*, Colombian author Gabriel García Márquez takes the reader to the mythical jungle village of Macondo, where, in one oft-recounted scene, residents suffer from a disease that causes them to lose all memory. The malady erases “the name and notion of things and finally the identity of people.” The symptoms persist until a traveling gypsy turns up with a drink “of a gentle color” that returns them to health.

In a 21st-century parallel to the townspeople of Macondo, a few hundred residents from Medellín, Colombia, and nearby coffee-growing areas may get a chance to assist in the search for something akin to a real-life version of the gypsy's concoction. Medellín and its environs are home to the world's largest contingent of individuals with a hereditary form of Alzheimer's disease. Members of 25 extended families, with 5,000 members, develop early-onset Alzheimer's, usually before the age of 50, if they harbor an aberrant version of a particular gene.

Early-onset Alzheimer's, passed down as a dominant genetic trait from only one parent, accounts for less than 1 percent of the 27 million Alzheimer's cases worldwide documented in 2006, but its hallmark brain lesions appear to be

identical to those in the more common late-onset form, in which symptoms do not appear until after the age of 65.

The predictability of disease onset in the Medellín families has attracted the attention of a group of scientists and pharmaceutical companies who are considering a novel approach to research that will test drugs in patients before the first signs of dementia appear.

In recent years a number of drug candidates for treating mild or moderate Alzheimer's have failed, persuading researchers that much of the disease pathology—accretions of aberrant proteins and loss of brain cells or circuits—begins well before the memory loss becomes apparent. This growing realization, confirmed by new technologies that can track the disease years before the first symptom, suggests that to be most successful, treatment must start during the many years when the insidious disease process is already under way, even though a patient's memory remains intact.

Consequently, a major thrust of much Alzheimer's research is shifting toward arresting the disease in advance of symptoms—not only with drugs but also with lifestyle measures that would be safer and less costly than filling a drug prescription for 10 or 20 years.

**Interventions before symptoms appear could be key to slowing or stopping the leading cause of dementia**

**By Gary Stix**

## KEY CONCEPTS

- The incidence of Alzheimer's disease continues to rise as the population ages, but effective treatments are lacking.
- Some new drugs may have failed because they were tried too late.
- New techniques to track the disease before symptoms arise may allow testing of drugs at a stage when they may be more effective.

—The Editors



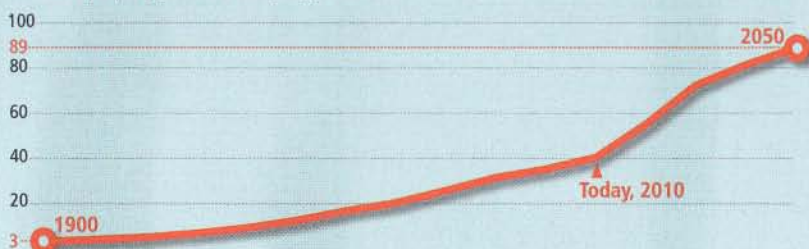
## [ALZHEIMER'S NUMBERS]

# THE COMING FLOOD

As the U.S. population ages—along with that of the rest of the world—the number of new Alzheimer's cases will soar because the incidence increases with age. In 2010 an estimated 39 million people in the U.S. are senior citizens, a figure that will more than double to 89 million by 2050.

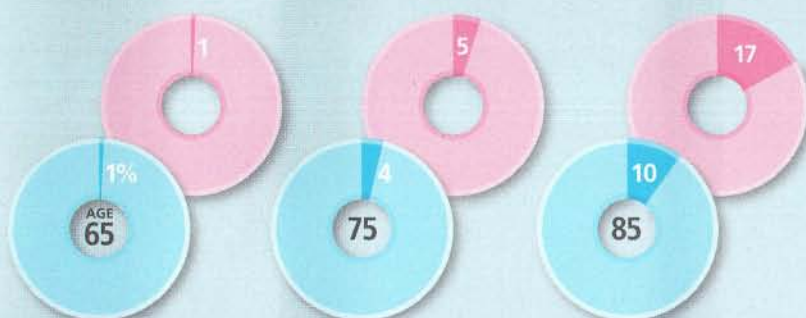
### THE POPULATION IS AGING ...

Millions of people aged 65 and older, living in the U.S.



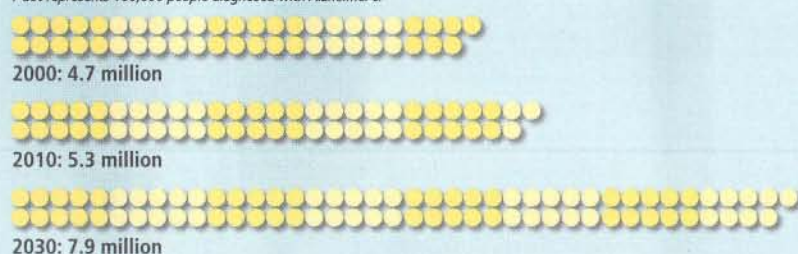
### ... AND AGE IS THE BIGGEST RISK FACTOR FOR ALZHEIMER'S ...

Risk of developing Alzheimer's at a given age over the next 10 years, for males and females.



### ... SO THE NUMBER OF CASES IS GROWING

Numbers of people diagnosed with Alzheimer's will increase by nearly 50 percent during the next 20 years. 1 dot represents 100,000 people diagnosed with Alzheimer's.



## An Early Start

The Colombian Alzheimer's families stand in the vanguard of prevention research. Francisco Lopera, the neurologist who 28 years ago first came across the families who were later discovered to bear the *paisa* mutation (named after the moniker for the people of the region), has begun to contact hundreds of still healthy family members. He wants to probe their willingness to participate in a test of drugs that would remove or stop the buildup of toxic protein fragments, amyloid-beta peptides, that damage brain cells early in the disease process. "The contribution made by these families may shed a lot of light on the treatment and prevention of both early- and late-life Alzheimer's," Lopera says.

In the planned trial, which could begin as early as next year and is part of a broader effort called the Alzheimer's Prevention Initiative (API), healthy, mutation-bearing family members around the age of 40 would start to receive anti-amyloid therapies (a drug or vaccine) already tested for safety in Alzheimer's patients. Talks are under way to send a cyclotron—a small particle accelerator—to be shared by a group of hospitals in Medellín for making radioactive tracers needed for imaging studies that would reveal whether the drug is hindering amyloid buildup.

The trial will evaluate whether a treatment can delay or stop the inexorable silent progression of the disease if administered seven years before the average age of diagnosis in family members who carry the gene. Beyond testing specific therapies, the designers of the Colombian trials also plan to see whether tracking of Alzheimer's-specific biomarkers can indicate whether an experimental treatment is working. (A biomarker is a measurable indicator—such as a concentration of a particular protein—that changes in concert with progression or regression of a disease.) A reliable set of biomarkers would allow drug researchers and clinicians caring for patients to evaluate success of a therapy relatively quickly, by measuring changes in such silent benchmarks, instead of having to wait to assess overt symptoms. The API plans to undertake a similar set of trials with a U.S.-based group made up of carriers of two copies of a gene variant, *APOE4*, that increases susceptibility to Alzheimer's, although carriers are not guaranteed to get the disease.

If successful, the API would serve as a model for making biomarker-based Alzheimer's prevention trials commonplace. Proving that a drug prevents a disease takes much longer and costs





much more than ascertaining whether it works in a patient who is already sick. "A pharmaceutical company is not going to invest in the longer duration of a prevention trial for an unproven agent that may not be efficacious," notes Maria Carrillo, senior director of medical and scientific relations for the Alzheimer's Association.

With a set of biomarkers in hand, a pharmaceutical company could test whether a drug changes levels of amyloid or another biomarker in the same way that physicians test cholesterol levels as a gauge of whether a statin is helping to prevent heart disease. "We need to move pre-symptomatic treatments forward. Otherwise we could lose a whole generation," says Eric M. Reiman, executive director of the Banner Alzheimer's Institute in Phoenix, who, along with colleague Pierre N. Tariot, launched the API.

The challenges of prevention trials still loom large: the drawbacks posed by inevitable drug side effects are more difficult to weigh against potential benefits in patients who do not yet have symptoms. Moreover, no one can predict whether a drug that proves helpful for early-onset Alzheimer's will also work in patients who lack the particular gene mutation that brings on the early-onset form of the disease. But the urgency of finding new treatments—and the lure of a multi-billion-dollar drug—has given momentum to prevention strategies. An organizational meeting for the API in January drew 19 U.S. and European pharmaceutical and biotechnology companies to a Phoenix airport hotel to discuss the possibility of forming a noncompetitive partnership in which academics and industry would collaborate on clinical studies and share results freely.

Some therapies for Alzheimer's do exist, but they do little to delay disease progression. A true disease-modifying treatment would meet with overwhelming patient demand. Statisticians predict that by the middle of the century, the global prevalence of Alzheimer's will quadruple, reaching 107 million. A treatment that delays disease onset by even five years would halve the number of people who die from the disease.

## Inside Your Head

An Alzheimer's prevention trial based on biomarkers would have been dismissed as fantasy as recently as five years ago. Such an endeavor may come to fruition because imaging and other technologies, now flourishing worldwide, can track biomarkers to reveal the nature of the underlying disease process. In the U.S. since 2004, the Alzheimer's Disease Neuroimaging

Initiative (ADNI), a collaboration among pharmaceutical companies, academics and the National Institutes of Health, has been developing methods to better assess the effectiveness of drugs tested in individuals suffering from the disease, a goal that quickly expanded to look at what is happening during the time before an actual diagnosis is made.

One intriguing report of progress in the field came January 21, when Clifford R. Jack, head of the group within ADNI studying biomarkers that can be detected with magnetic resonance imaging (MRI), described a model of how the disease likely progresses and paired it with biomarkers that seem able to track this pathology. Jack presented his work, which also appeared in a technical paper, to an online audience of more than 100 people during a Web seminar on Alzforum, a gathering that included many leading researchers in the field. Co-founded by June Kinoshita, a former *Scientific American* editor, Alzforum is a meeting place for the exchange of ideas, a repository of research information and a source of perhaps the most in-depth journalism anywhere on Alzheimer's research.

At the Web seminar, Jack noted that the biomarker measurements have demonstrated that the disease process begins years before the defining symptoms that allow a diagnosis to be made. During this time (estimated to range from five to 20 years), a particular type of amyloid peptide

## 100 YEARS OF RESEARCH

**1906:** German psychiatrist Alois Alzheimer first describes (based on a brain autopsy) the extracellular plaques and the tangles in neurons that characterize the disease.

### The Next 50 Years:

Memory loss and other symptoms are regarded as the senility that results from normal aging.

**1960s:** A link is established between cognitive decline and the number of plaques and tangles in the brain.

**1980s:** Researchers start to unravel the fundamental biochemistry that leads to plaques and tangles.

**1990s:** Several discoveries identify genetic factors underlying the disease, and the first drugs that improve symptoms come to market.

**2000s:** Imaging and spinal fluid samples enable scientists to track the disease course. A number of drugs that target disease processes fail in clinical trials, leading many to conclude that earlier treatment is needed.

### [TODAY'S DRUGS]

## Some Relief, But Not Enough

Current drugs treat cognitive symptoms only, not the underlying disease process, and work for a limited time, from months to a few years.

#### DRUG CLASS:

Acetylcholinesterase inhibitor  
(Examples: donepezil, galantamine)

#### What It Does:

Blocks the action of an enzyme, acetylcholinesterase, thereby increasing levels of the brain chemical acetylcholine. Extra acetylcholine improves cognition, mood and behavior and so promotes better daily functioning.

#### DRUG CLASS:

NMDA receptor antagonist  
(One drug: memantine)

#### What It Does:

Helps to quell overactivity by a signaling chemical, glutamate, that can lead to the death of neurons. The drug does not interfere with the buildup of cell lesions that may drive progression of the disease.





[PROGRESS TOWARD PREVENTION]

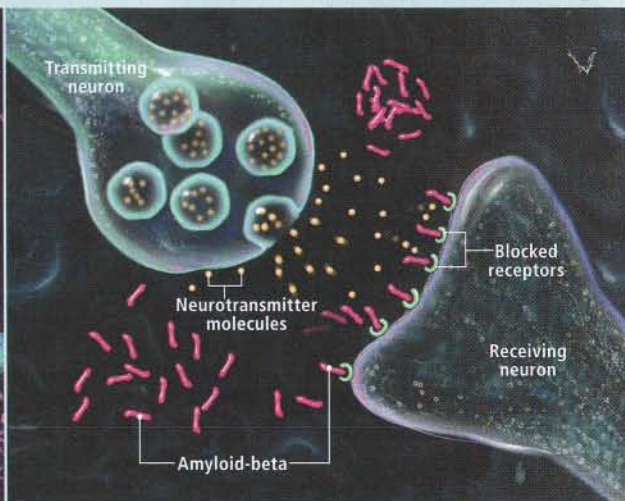
# NEW TOOLS DETECT SILENT EARLY SIGNS

The disease process underlying Alzheimer's (*below*) starts years before symptoms would lead to a diagnosis. Researchers can now track it in living patients with tools—including brain imaging and spinal fluid tests (*far right*)—that monitor Alzheimer's-related biomarkers: signs of biological changes (such as mounting levels of toxic proteins) that routinely occur in the course of the disease. Researchers hope that one day biomarker testing will identify incipient disease in people and that treatment in this early stage will delay or prevent dementia.

## AMYLOID ACCRETION

5–20 years before diagnosis of Alzheimer's dementia

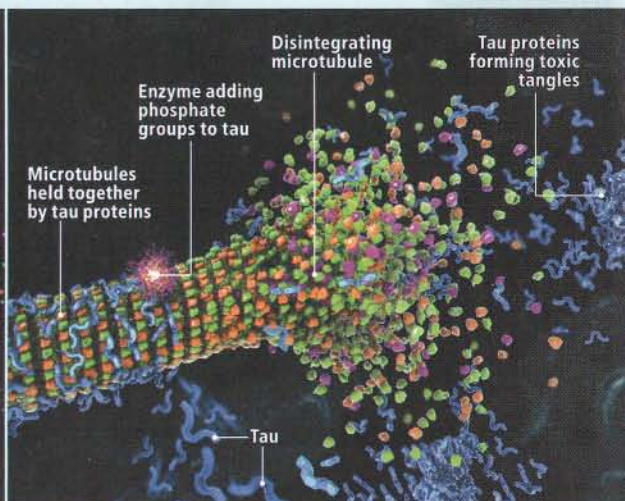
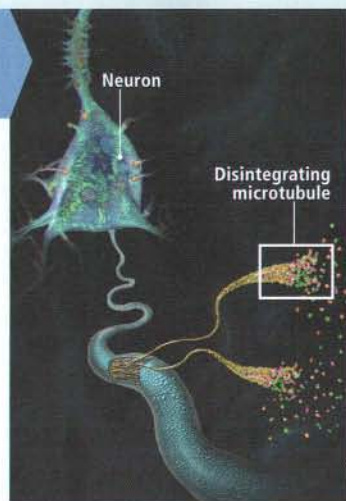
Early on, a protein fragment called amyloid-beta aggregates in the brain centers that form new memories. The amyloid buildup, a biomarker detected by the presence of plaques, results in damage to synapses, the interface between neurons (*detail*). Amyloid blocks chemical signals (neurotransmitters) from reaching receptors on receiving neurons. This buildup can be captured by various forms of neuroimaging, including positron-emission tomography (PET), that detect a radioactive compound, Pittsburgh imaging compound-B (PIB), able to bind specifically to amyloid. A spinal tap can also be used to gauge the amyloid biomarker.



## TAU BUILDUP

1–5 years before diagnosis

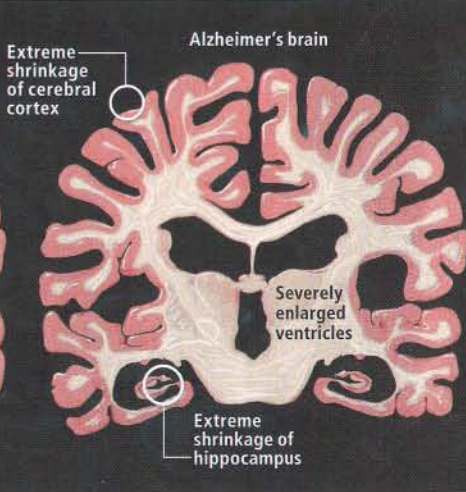
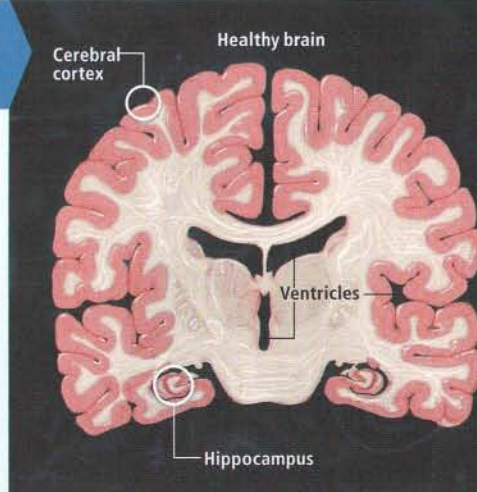
Before symptoms would justify an Alzheimer's diagnosis, a protein called tau inside neurons begins misbehaving. Normally tau helps to maintain the structure of tiny tubes (microtubules) critical to the proper functioning of neurons. But now phosphate groups begin to accumulate on tau proteins (*detail*), which detach from the microtubules. The tubules go on to disintegrate, and tau then aggregates, forming tangles that interfere with cellular functions. A sample of spinal fluid can detect this process.



## BRAIN SHRINKAGE

1–3 years before diagnosis

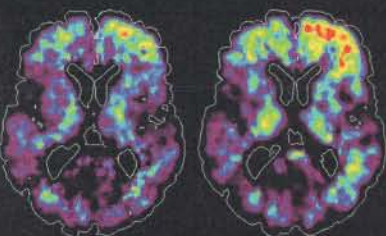
As the underlying disease process advances, nerve cells start to die, and patients and family notice memory and other cognitive lapses. Cell death shrinks the brain in areas that involve memory (the hippocampus) and higher-level brain functions (the cortex) and thus can be tracked with a form of magnetic resonance imaging that measures brain volume. Such shrinkage accelerates and ultimately involves many areas of the brain.





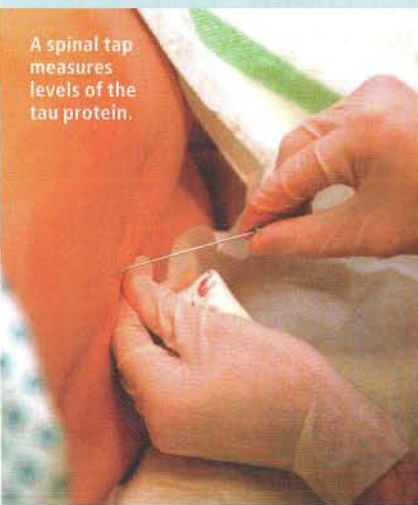
## BIOMARKER TECHNOLOGIES

Baseline 24 months

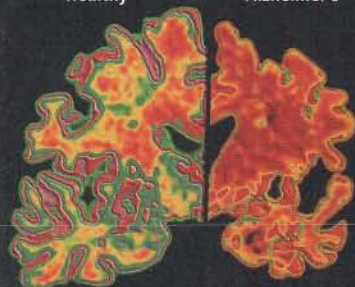


PET scans show increasing retention in the brain's frontal lobes of the amyloid-beta tracer PIB over the course of two years in a 74-year-old, even while the subject remained cognitively normal.

A spinal tap measures levels of the tau protein.



Healthy Alzheimer's



Computer graphic of slices through a normal brain and an Alzheimer's brain, derived from volumetric magnetic resonance imaging, shows considerable shrinkage (right) from degeneration and death of nerve cells.

COURTESY OF THE UNIVERSITY OF PITTSBURGH AMYLOID IMAGING GROUP (PET); DAVID HOFFMAN PHOTO LIBRARY (spinal tap); A. PAKIEKA PHOTO RESEARCHERS, INC. (brain comparison); BASED ON A PRESENTATION BY CLIFFORD B. JACK OF THE MAYO CLINIC

begins to aggregate outside of brain cells and damage synapses, the contact points between neurons. A radioactive tracer molecule, such as Pittsburgh imaging compound-B (PIB), can bind to amyloid in a patient's brain and then be imaged using PET (positron-emission tomography). The imaging technique, abbreviated PIB-PET, has shown that this aggregation process starts to level off before definitive symptoms arise.

Later on, but also before a diagnosis, a class of proteins called tau, which normally assist in providing structural support to neurons, become detached from the cells' scaffolding and clump into tangles, wreaking havoc inside the cells. The tau buildup can be detected by examining a sample of cerebrospinal fluid. This test can also look for decreasing levels of amyloid-beta, which occur as the peptides get removed from the fluid to form deposits in the brain. Together, decreasing levels of amyloid-beta and an increase in tau in the cerebrospinal fluid give a strong signal that the disease process is advancing.

Anywhere from one to four years before a person is diagnosed with Alzheimer's, a phase called mild cognitive impairment sets in. It is characterized by symptoms that range from memory lapses to poor decision making. Mild cognitive impairment can arise from causes other than Alzheimer's, but in those who are on the road to Alzheimer's dementia, mild cognitive impairment occurs because neurons in certain brain areas are damaged or dying—a loss that accelerates over time. (If memory problems are the primary symptom, the patient often progresses to Alzheimer's.) This stage can be tracked with a form of imaging called volumetric MRI, which measures shrinkage of the brain as neurons expire. The cascade of events, including the early accretion of amyloid, disrupts cell metabolism and can be monitored with a form of PET, fluorodeoxyglucose-PET (FDG-PET), that gauges the metabolic status of neurons.

### But Does the Patient Get Better?

Using biomarkers as the basis of clinical trials for prevention poses a set of challenges to both pharmaceutical companies and regulators—and constitutes a barrier to moving ahead with the API and other prevention efforts. To be approved, an Alzheimer's drug needs to show that it provides cognitive benefits for the patient (in memory, language or a related measure) better than a placebo does.

If a biomarker is tracked instead of symptoms in a prevention study, researchers need to be sure

that the measurements truly presage whether a subject is likely to develop dementia. For instance, investigators do not yet know whether changing amyloid-beta levels will ultimately prevent dementia, despite the large body of evidence suggesting that amyloid-beta contributes to disease development.

In fact, in one early trial of an amyloid therapy, the levels of the peptide decreased in some patients, but there was almost no evidence that cognition improved. "We're concerned that we might have a drug that affects a marker in the way that we predict but that it doesn't affect patients' clinical picture," says Russell Katz, director of the division of neurology products for the Food and Drug Administration. "In other words, their disease continues to progress, and they don't get any better." Katz says a better approach to incorporating biomarkers in clinical trials would be to first show that reducing levels of amyloid or another biomarker benefits patients who have mild cognitive impairment or who are newly diagnosed with Alzheimer's and to attempt to use biomarkers in people without symptoms only afterward. "The best way to get there in my opinion is to start with patients who have symptoms, maybe very, very early patients, and then work backward," Katz says.

But the researchers in the Colombian prevention trials assert that they may already be capable of using biomarkers to detect subtle changes in memory, thereby allaying Katz's concern. And Reiman cites work from his group that might offer another way to help ease regulator concerns. In that study, carriers of the APOE4 gene variant showed a small decline in scores for memory on psychological tests many years before any cognitive deficit became noticeable. This level of sensitivity, Reiman says, means that applying a cognitive test along with a biomarker measure in a prevention trial might suffice to indicate, say, whether prospects for avoiding dementia really do improve as amyloid levels drop. For the moment, Katz still needs convincing. "What is the evidence that these patients, despite their diminished cognitive status, will actually go on to develop Alzheimer's?"

Some companies are already trying to gain a better understanding of how to use biomarkers. Bristol-Myers Squibb has been sampling the spinal fluid of patients with mild cognitive impairment to try to predict which ones are likely to progress to Alzheimer's. Those who exhibit a low level of amyloid-beta and a high level of tau will be qualified to participate in a trial of a drug



[STATE OF THERAPY]

# WHY TREATMENTS LAG

**A**ny drug that substantively delayed or stopped Alzheimer's would be an immediate blockbuster, perhaps exceeding sales for Prozac or Lipitor. No such drugs are on the market because investigators are still trying to understand how to alter the underlying mechanisms by which the disease causes dementia.

Drugs that impede amyloid buildup offer a case in point: a number of drug possibilities at various stages of testing can purportedly inhibit amyloid accumulation or foster its clearance. Yet several anti-amyloid drugs tested in clinical trials have already failed. (The table below lists major classes of Alzheimer's drugs under development.) Some researchers wonder whether too little emphasis has been placed on interfering with other processes that contribute to the disorder. Among the 100 or so agents under development are prospective drugs that target the cell-damaging tau protein. Some are intended to quell inflammation, boost the functioning of mitochondria, enhance cerebral insulin levels or provide other protection for neurons. The most recent high-profile failure involved Dimebon, a drug that did not target amyloid. As with cancer and HIV, it may be necessary to combine several of these agents to slow or halt Alzheimer's. —G.S.

## DRUGS UNDER STUDY WHAT THEY DO

Inhibitors of enzymes that produce amyloid-beta	Such inhibitors block or modify the action of enzymes that cut a large protein (the amyloid precursor protein) in a way that releases the amyloid-beta peptides.
Vaccines or antibodies that clear amyloid-beta	Vaccines induce the body to produce antibodies that bind to amyloid and clear them from the brain. Unfortunately, in clinical trials, both vaccines and antibodies have induced side effects of varying severity in some patients.
Amyloid-beta aggregation blockers	Agents that prevent amyloid fragments from clumping could prevent damage to neurons.
Antitau compounds	These agents, although fewer in number than those that target the amyloid pathway, take various approaches, such as blocking production of the toxic form of the tau protein or impeding its aggregation into tangles.
Neuroprotective agents	Different strategies attempt to boost natural brain chemicals that enhance the health of neurons. In one, a gene is delivered into the brain to start production of a protective substance.

**Absent effective drugs, some researchers and clinicians are exploring diet along with mental and physical exercise as preventive steps.**

that blocks an enzyme, called gamma secretase, involved in producing the amyloid-beta peptide. "If you don't have the biomarker associated with Alzheimer's pathophysiology, you won't be eligible to be enrolled into the treatment arm of our study," notes Vlad Coric, medical director for global science clinical research at Bristol-Myers Squibb. The ability to target only the patients who are more likely to get a diagnosis of Alzheimer's will facilitate assessment of whether the drug really works, results that would be less clear if the trial had included participants who have little chance of getting the disease. "Looking into the future, one would perhaps start drug trials even earlier, during the presymptomatic phase," Coric adds.

### A Cognitive Shop

The Colombian Alzheimer's families at the center of the API have also served as inspiration for another innovative approach to prevention. Neu-

roscientist Kenneth S. Kosik, who has worked with the Colombian families for nearly 20 years and who helped to identify the *paisa* mutation, established last year what he calls a "cognitive shop" in a residential neighborhood of Santa Barbara, Calif. It was Kosik who arranged a pivotal meeting in Medellín to bring Lopera and the Colombian families into the API.

The cognitive shop—known more formally as the center for Cognitive Fitness & Innovative Therapies (CFIT)—is a refuge for both those with the mild memory complaints that sometimes precede full-fledged Alzheimer's and the worried well. They go to the Mediterranean-style building to receive advice, based on the best existing evidence, about life changes they can make to perhaps help ward off the specter of dementia—or to better cope with it if it does arrive.

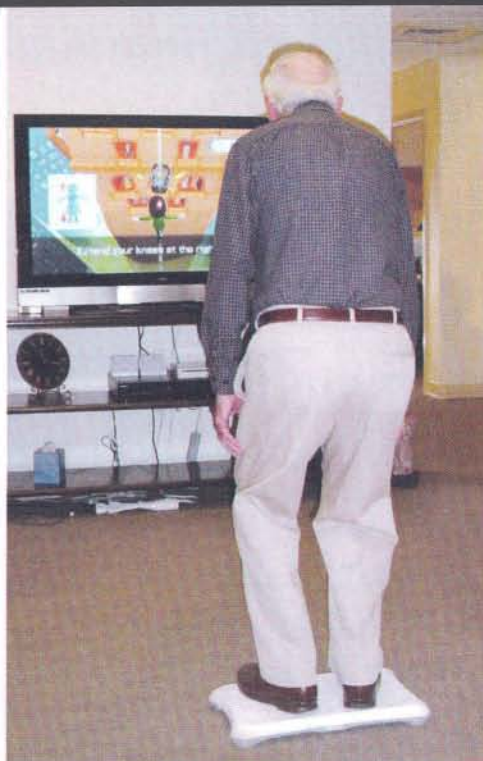
Kosik took the idea for CFIT from Casa Neurociencias, a less sumptuous outpatient clinic near the central hospital in Medellín, a place he spent many hours working alongside Lopera. Alzheimer's patients with the *paisa* mutation, along with, at times, dozens of family members, would take a long bus ride from the countryside to spend the day in the clinic's open space, where the medical staff and family members had easy access to one another. "It was remarkable that there, where the medical system was not so developed, the caring side and the ancillary services were more available," Kosik says.

During his trips, Kosik contrasted the atmosphere favorably to the clinical efficiency of Harvard Medical School, where he had co-founded a memory disorders clinic at Brigham and Women's Hospital before moving to the University of California, Santa Barbara, in 2004. "I developed a frustration with the fact that people would come into the clinic and we would say, yes, this is looking like Alzheimer's, and then it was *adios*," he says. "We would see them and follow up every six months, but we couldn't do much except document their decline."

CFIT combines the informality of Casa Neurociencias with lifestyle recommendations, much of them based on a still evolving body of scientific evidence derived from recent epidemiological or animal studies suggesting that different behaviors might aid cognition. Epidemiologists follow a selected group to determine whether exercise, diet or a multitude of other activities might reduce the risk of a disease such as Alzheimer's, although more rigorous types of studies are needed to make definitive conclusions.

After a physical and psychological evalua-





tion, a client (the word “patient” is never used) receives a series of personalized recommendations that may include adopting the Mediterranean diet (healthy fats and high fruit and vegetable consumption), engaging in aerobic exercise and playing online brain games. The center engages in some activities that have yet to become standard practice at places such as the Harvard-affiliated memory clinic. As an acknowledgment of the reality of a new era in which patients want more control of their medical care, Tonya Kydland, a cognitive psychologist, acts as a “navigator” to guide people through the morass of medical information on the Internet. She projects a large image of a Web browser on a wall of a darkened conference room and takes a client, page by page, through clinical trials or recent studies on curcumin or another dietary supplement purported to protect brain cells, explaining the weight of evidence for one compound versus another.

CFIT also undertakes the controversial practice of coordinating testing for the *APOE4* gene variant. The test is done after counseling the client about the implications of learning the results: if positive, siblings and children may also carry the same gene version and thus be at higher risk. Medical groups discourage testing because knowing one’s gene status does not allow a definite prediction about getting Alzheimer’s, and effective treatments do not exist.

Kosik, who was a co-author of one of the early papers on the toxic tau protein, denies that he has become a “hot tub” physician who endorses flaky ideas. His laboratory at U.C. Santa Barbara still does studies on the tau protein and other

esoteric basic biology. CFIT is intended to fill the gap until the API or some other venture can uncover drugs or other measures that have been proved to work. “The solutions we have here are ultimately not the best solution,” Kosik comments. “But we don’t know when a drug is going to arrive that treats the disease the same way penicillin treats an infection. I think it’s irresponsible to tell people it’s going to be five or 10 years, because I don’t think we know that.”

In coming years, CFIT’s approach to prevention will receive closer scrutiny in rigorous government-funded clinical trials designed to find out whether diet and exercise can really delay the disease or whether the evidence from the epidemiology was just a statistical fluke. One major question for the lifestyle work, says Reisa Sperling, associate professor of neurology at Harvard Medical School, is whether interventions have different effects in people whose brains are currently normal than in those already showing Alzheimer’s-related changes. “Some of these interventions may modulate risk, but if you’re already on the road—if you’ve got the genes, and you’ve already got a head full of amyloid—these interventions may be less able to slow the progression, and so it’s important to test these ideas using biomarkers to see if they really work.”

Ultimately, PET technology or a lumbar puncture may determine whether olives, goat cheese and half an hour every day on the treadmill help to preserve cognition or are just a mere chimera. If such biomarkers do prove useful, biological and behavioral research may finally come together into a true science of Alzheimer’s prevention. ■

#### IMPORT FROM COLOMBIA:

Neurologist Francisco Lopera (pointing his left finger) established a standard of care for the world’s largest contingent of families with a hereditary form of Alzheimer’s disease at a clinic in Medellín, Colombia. The community-centered treatment approach instituted by Lopera and his colleagues served as an inspiration for a “cognitive shop” in Santa Barbara (right), where clients engage in programs of physical exercise and other activities aimed at reducing the risk of dementia.

#### ➔ MORE TO EXPLORE

**The Alzheimer’s Project: Momentum in Science.** Based on the HBO documentary. John Hoffman and Susan Froemke, with Susan K. Golant. Public Affairs Books, New York, 2009.

**The Alzheimer’s Solution: How Today’s Care Is Failing Millions and How We Can Do Better.** Kenneth S. Kosik and Ellen Clegg. Prometheus Books, 2010.

Gabrielle Strobel of Alzforum led a discussion on January 21 about disease-tracking “biomarkers” with a number of leading researchers: [www.alzforum.org/res/for/journal/detail.asp?liveID=179](http://www.alzforum.org/res/for/journal/detail.asp?liveID=179)



# PHYSICS



**DYNAMISM FROM STASIS:** The art of Keith Peters explores the idea that an inherently static world can nonetheless evoke dynamism.





# Is Time an ILLUSION?

The concepts of time and change may emerge from a universe that, at root, is utterly static

By Craig Callender

**A**s you read this sentence, you probably think that this moment—right now—is what is happening. The present moment feels special. It is real. However much you may remember the past or anticipate the future, you live in the present. Of course, the moment during which you read that sentence is no longer happening. This one is. In other words, it feels as though time flows, in the sense that the present is constantly updating itself. We have a deep intuition that the future is open until it becomes present and that the past is fixed. As time flows, this structure of fixed past, immediate present and open future gets carried forward in time. This structure is built into our language, thought and behavior. How we live our lives hangs on it.

Yet as natural as this way of thinking is, you will not find it reflected in science. The equations of physics do not tell us which events are occurring right now—they are like a map without the “you are here” symbol. The present moment does not exist in them, and therefore neither does the flow of time. Additionally, Albert Einstein’s theories of relativity suggest not only that there is no single special present but also that all moments are equally real [see “That Mysterious Flow,” by Paul Davies; *SCIENTIFIC AMERICAN*, September 2002]. Fundamentally, the future is no more open than the past.

The gap between the scientific understanding of time and our everyday understanding of time has troubled thinkers throughout history. It has widened as physicists have gradually stripped time of most of the attributes we commonly ascribe to it. Now the rift between the time of physics and the time of experience is reaching its logical conclusion, for many in theoretical physics have come to believe that time fundamentally does not even exist.

The idea of a timeless reality is initially so startling that it is hard to see how it could be coherent. Everything we do, we do in time. The world is a series of events strung together by time. Any-

## KEY CONCEPTS

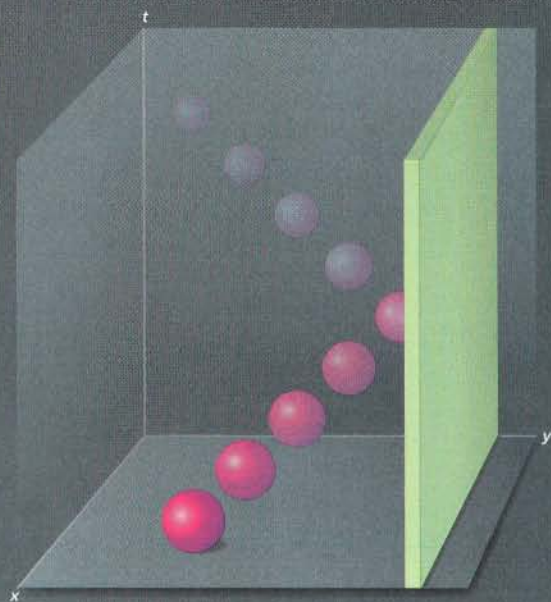
- Time is an especially hot topic right now in physics. The search for a unified theory is forcing physicists to reexamine very basic assumptions, and few things are more basic than time.
- Some physicists argue that there is no such thing as time. Others think time ought to be promoted rather than demoted. In between these two positions is the fascinating idea that time exists but is not fundamental. A static world somehow gives rise to the time we perceive.
- Philosophers have debated such ideas since before the time of Socrates, but physicists are now making them concrete. According to one, time may arise from the way that the universe is partitioned; what we perceive as time reflects the relations among its pieces. —The Editors

KEITH PETERS

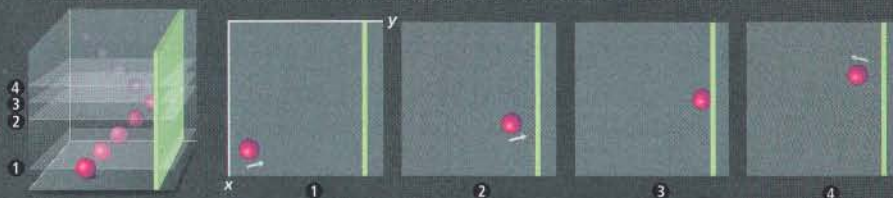


# How Time Is Not Like Space

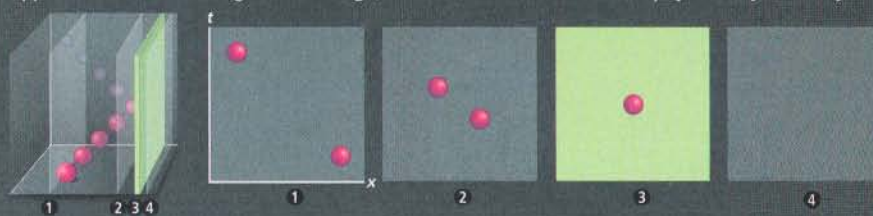
Physicists, artists and graph makers of all kinds routinely depict time as another dimension of space, creating a unified spacetime—shown here as a three-dimensional block in which a ball bounces off a wall. Relativity theory holds that spacetime can be sliced up in various ways. But not all are equally sensible.



The usual way takes slices of space at successive moments of time, creating a movie of the ball's motion. Each frame leads to the next, according to the familiar laws of physics.



An alternative considers slices not from past to future but from left to right. Each slice is part space, part time. To the left of the wall, the ball appears in two positions; on the right, it does not appear at all. If this slicing seems strange, it should: it makes the laws of physics very unwieldy.



one can see that my hair is graying, that objects move, and so on. We see change, and change is the variation of properties with respect to time. Without time, the world would be completely still. A timeless theory faces the challenge of explaining how we see change if the world is not really changing.

Recent research attempts to perform just this feat. Although time may not exist at a fundamental level, it may arise at higher levels—just as a table feels solid even though it is a swarm of particles composed mostly of empty space. Solidity is a collective, or emergent, property of the particles. Time, too, could be an emergent property of whatever the basic ingredients of the world are.

This concept of emergent time is potentially as revolutionary as the development of the theories of relativity and of quantum mechanics a century ago. Einstein said that the key step forward in developing relativity was his reconceptualization of time. As physicists pursue his dream of unifying relativity with quantum mechanics, they believe that time is again central. In 2008 the Foundational Questions Institute (FQXi) sponsored an essay contest on the nature of time, and a veritable who's who of modern physics weighed in. Many held that a unified theory will describe a timeless world. Others were loath to get rid of time. The one thing they agreed on was that without thinking deeply about time, progress on unification may well be impossible.

## The Rise and Fall of Time

Our rich commonsensical notions of time have suffered a withering series of demotions throughout the ages. Time has many jobs to do in physics, but as physics has progressed, these jobs have been outsourced one by one.

It may not be obvious at first, but Isaac Newton's laws of motion require time to have many specific features. All observers in principle agree on the sequence in which events happen. No matter when or where an event occurs, classical physics assumes that you can objectively say whether it happens before, after or simultaneously with any other event in the universe. Time therefore provides a complete ordering of all the events in the world. Simultaneity is absolute—an observer-independent fact. Furthermore, time must be continuous so that we can define velocity and acceleration.

Classical time must also have a notion of duration—what physicists call a metric—so that we can tell how far apart in time events are from one another. To say that Olympic sprinter Usain Bolt can run as fast as 27 miles per hour, we need to have a measure of what an hour is. Like the order of events, duration is observer-independent. If Alice and Bob leave school at 3 o'clock, go their separate ways, and then meet back at home at 6 o'clock, the amount of time that has elapsed for Alice is equal to the amount of time that has elapsed for Bob.

Without thinking deeply about time, physicists may never make progress on a unified theory.



In essence, Newton proposed that the world comes equipped with a master clock. The clock uniquely and objectively carves the world up into instants of time. Newton's physics listens to the ticking of this clock and no other. Newton additionally felt that time flows and that this flow gives us an arrow telling us which direction is the future, although these extra features are not strictly demanded by his laws.

Newton's time may seem old hat to us now, but a moment's reflection reveals how astonishing it is. Its many features—order, continuity, duration, simultaneity, flow and the arrow—are logically detachable, yet they all stick together in the master clock that Newton dubbed “time.” This assembly of features succeeded so well that it survived unscathed for almost two centuries.

Then came the assaults of the late 19th and early 20th centuries. The first was the work of Austrian physicist Ludwig Boltzmann, who reasoned that, because Newton's laws work equally well going forward or backward in time, time has no built-in arrow. Instead he proposed that the distinction between past and future is not intrinsic to time but arises from asymmetries in how the matter in the universe is organized. Although physicists still debate the details of this proposal [see “The Cosmic Origins of Time's Arrow,” by Sean M. Carroll; *SCIENTIFIC AMERICAN*, June 2008], Boltzmann convincingly plucked away one feature of Newtonian time.

Einstein mounted the next assault by doing away with the idea of absolute simultaneity. According to his special theory of relativity, what events are happening at the same time depends on how fast you are going. The true arena of events is not time or space, but their union: spacetime. Two observers moving at different velocities disagree on when and where an event occurs, but they agree on its spacetime location. Space and time are secondary concepts that, as mathematician Hermann Minkowski, who had been one of Einstein's university professors, famously declared, “are doomed to fade away into mere shadows.”

And things only get worse in 1915 with Einstein's general theory of relativity, which extends special relativity to situations where the force of gravity operates. Gravity distorts time, so that a second's passage here may not mean the same thing as a second's passage there. Only in rare cases is it possible to synchronize clocks and have them stay synchronized, even in principle. You cannot generally think of the world as unfolding, tick by tick, according to a single

time parameter. In extreme situations, the world might not be carvable into instants of time at all. It then becomes impossible to say that an event happened before or after another.

General relativity contains many functions with the English word “time” attached to them: coordinate time, proper time, global time. Together they perform many of the jobs Newton's single time did, but individually none of them seems worthy of the title. Either the physics does not listen to these clocks, or, if it does, those clocks apply only to small patches of the universe or to particular observers. Although physicists today fret that a unified theory will have to eliminate time, a good argument can be made that time was already lost by 1915 and that we just have not fully come to grips with it yet.

### Time as the Great Storyteller

What good is time, then? You might be tempted to think that the difference between space and time has nearly vanished and that the true arena of events in a relativistic universe is a big four-dimensional block. Relativity appears to spatialize time: to turn it into merely one more direction within the block. Spacetime is like a loaf of bread that you can slice in different ways, called either “space” or “time” almost arbitrarily.

Yet even in general relativity, time retains a distinct and important function: namely, that of locally distinguishing between “timelike” and “spacelike” directions. Timelike-related events are those that can be causally related. An object or signal can pass from one event to the other, influencing what happens. Spacelike-related events are causally unrelated. No object or signal can get from one to the other. Mathematically, a mere minus sign differentiates the two directions, yet this minus sign has huge effects. Observers disagree on the sequence of spacelike events, but they all agree on the order of timelike events. If one observer perceives that an event can cause another, all observers do.

In my own essay for the FQXi contest two years ago, I explored what this feature of time means. Imagine slicing up spacetime from past to future; each slice is the 3-D totality of space at one instant of time. The sum of all these slices of spacelike-related events is 4-D spacetime. Alternatively, imagine looking at the world sideways and slicing it up accordingly. From this perspective, each 3-D slice is a strange amalgam of events that are spacelike-related (in just two dimensions) and timelike-related. These two methods of slicing are like carving up a loaf of

#### [THE AUTHOR]



**Craig Callender** is a philosophy professor at the University of California, San Diego. Beginning with his Ph.D. thesis, *Explaining Time's Arrow*, he has explored the philosophy and physics of time, publishing scores of articles in physics and philosophy journals and editing books on both quantum gravity and time. He wrote the graphic text *Introducing Time* and is working on a book on the philosophy, physics and cognitive science of time entitled *Time: From the Inside Out*. He assures us that his lifelong interest in time has nothing to do with his last name.



bread either vertically or horizontally [see illustration on page 42].

The first method is familiar to physicists, not to mention moviegoers. The frames of a movie represent slices of spacetime: they show space at successive moments of time. Like film aficionados who instantly figure out the plot and predict what happens next, physicists can take a single complete spatial slice and reconstruct what happens on the other spatial slices, simply by applying the laws of physics.

The second method of slicing has no simple analogy. It corresponds to carving up spacetime not from past to future but from east to west. An example of such a slice might be the north wall in your house plus what will happen on that wall in the future. From this slice, you apply the laws of physics to reconstruct what the rest of your house (and indeed the rest of the universe) looks like. If that sounds strange, it should. It is not immediately obvious whether the laws of physics let you do that. But as mathematician Walter Craig of McMaster University and philosopher Steven Weinstein of the University of Waterloo have recently shown, you can, at least in some simple situations.

Although both methods of slicing are possible in principle, they are profoundly different. In the normal, past-to-future slicing, the data you need to collect on a slice are fairly easy to obtain. For instance, you measure the velocities of all particles. The velocity of a particle in one location is independent of the velocity of a particle someplace else, making both of them straightforward to measure. But in the second method, the particles' properties are not independent; they have to be set up in a very specific way, or else a single slice would not suffice to reconstruct all the others. You would have to perform extremely difficult measurements on groups of particles to gather the data you need. To make matters worse, only in special cases, such as the one Craig and Weinstein discovered, would even these measurements allow you to reconstruct the full spacetime.

In a very precise sense, time is the direction within spacetime in which good prediction is possible—the direction in which we can tell the most informative stories. The narrative of the universe does not unfold in space. It unfolds in time.

### Quantum Time

One of the highest goals of modern physics is to unite general relativity with quantum mechanics, producing a single theory that handles both

the gravitational and quantum aspects of matter—a quantum theory of gravity. One of the stumbling blocks has been that quantum mechanics requires time to have properties that contradict what I have said so far.

Quantum mechanics says that objects have a much richer repertoire of behaviors than we can possibly capture with classical quantities such as position and velocity. The full description of an object is given by a mathematical function called the quantum state. This state evolves continuously in time. Using it, physicists are able to calculate the probabilities of any experimental outcome at any time. If we send an electron through a device that will deflect it either up or down, quantum mechanics may not be able to tell us with certainty which outcome to expect. Instead the quantum state may give us only probabilities of outcomes; for instance, a 25 percent chance the electron will veer upward and a 75 percent chance it will veer downward. Two systems described with identical quantum states may give different outcomes. The outcomes of experiments are probabilistic.

The theory's probabilistic predictions require time to have certain features. First, time is that which makes contradictions possible. A rolled die cannot have both 5 and 3 facing up at the same time. It can do so only at different times. Connected to this feature is the fact that the probability of landing on each of the six numbers must add up to 100 percent, or else the concept of probability would not be meaningful. The probabilities add up at a time, not at a place. The same is true of the probabilities for quantum particles to have a given position or momentum.

Second, the temporal order of quantum measurements makes a difference. Suppose I pass an electron through a device that deflects it first along the vertical direction, then along the horizontal direction. As it emerges, I measure its angular momentum. I repeat the experiment, this time deflecting the electron horizontally, then vertically, and measuring its angular momentum again. The values I get will be vastly different.

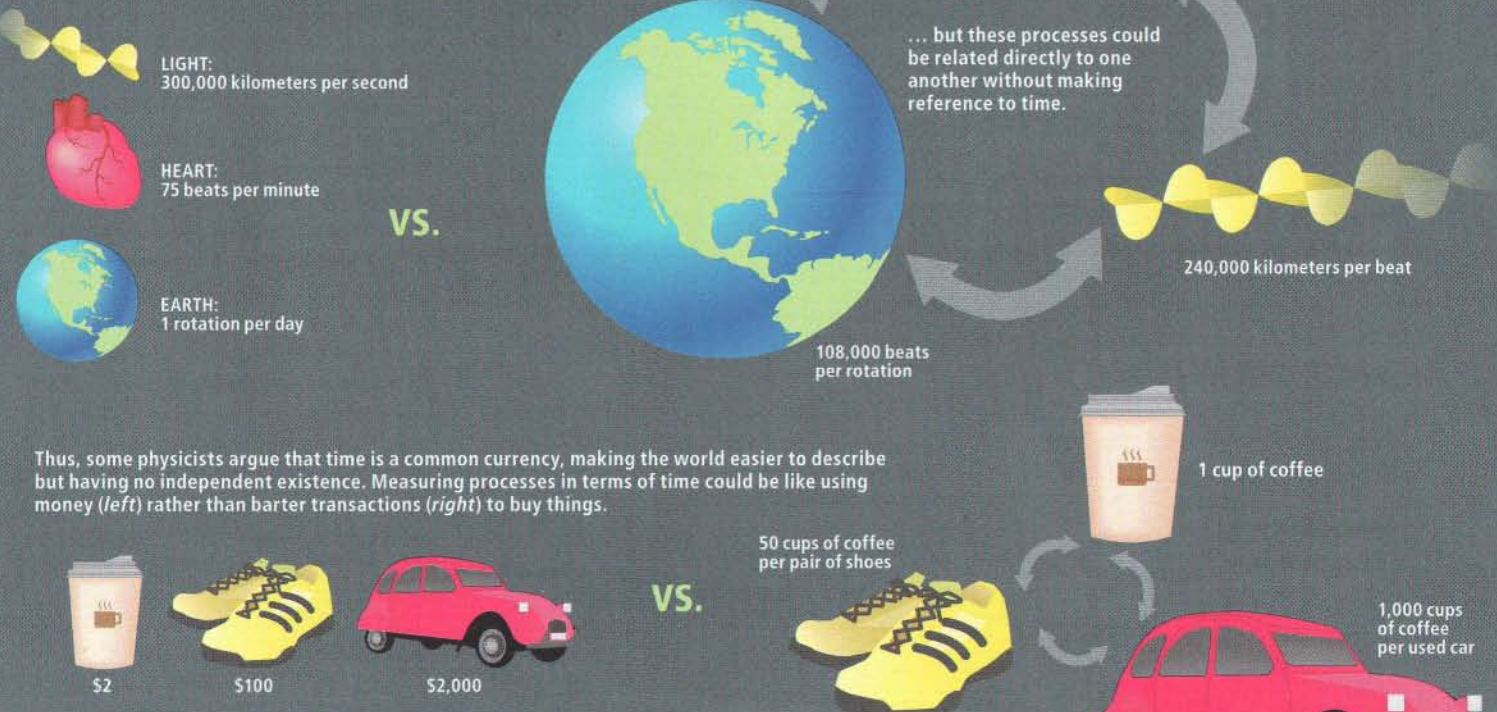
Third, a quantum state provides probabilities for all of space at an instant of time. If the state encompasses a pair of particles, then measuring one particle instantaneously affects the other no matter where it is—leading to the infamous “spooky action at a distance” that so troubled Einstein about quantum mechanics. The reason it bothered him was that for the particles to react at the same time, the universe must have a master clock, which relativity expressly forbids

Time  
is that  
which makes  
contradictions  
possible.



# Who Needs Time, Anyway?

Time is a way to describe the pace of motion or change, such as the speed of a light wave, how fast a heart beats, or how frequently a planet spins ...



Thus, some physicists argue that time is a common currency, making the world easier to describe but having no independent existence. Measuring processes in terms of time could be like using money (left) rather than barter transactions (right) to buy things.

[see "A Quantum Threat to Special Relativity," by David Z. Albert and Rivka Galchen; *SCIENTIFIC AMERICAN*, March 2009].

Although some of these issues are controversial, time in quantum mechanics is basically a throwback to time in Newtonian mechanics. Physicists fret about the absence of time in relativity, but perhaps a worse problem is the central role of time in quantum mechanics. It is the deep reason that unification has been so hard.

## Where Did the Time Go?

A large number of research programs have sought to reconcile general relativity and quantum mechanics: superstring theory, causal triangulation theory, noncommutative geometry, and more. They split roughly into two groups. Physicists who think quantum mechanics provides the firmer foundation, like superstring theorists, start with a full-blooded time. Those who believe that general relativity provides the better starting point begin with a theory in which time is already demoted and hence are more open to the idea of a timeless reality.

To be sure, the distinction between these two approaches is blurry. Superstring theorists have

recently investigated timeless theories [see "A Simple Twist of Fate," by George Musser, on page 9]. But to convey the basic problem that time poses, I will focus on the second approach. The leading instance of this strategy is loop quantum gravity [see "Atoms of Space and Time," by Lee Smolin; *SCIENTIFIC AMERICAN*, January 2004], which descends from an earlier program known as canonical quantum gravity.

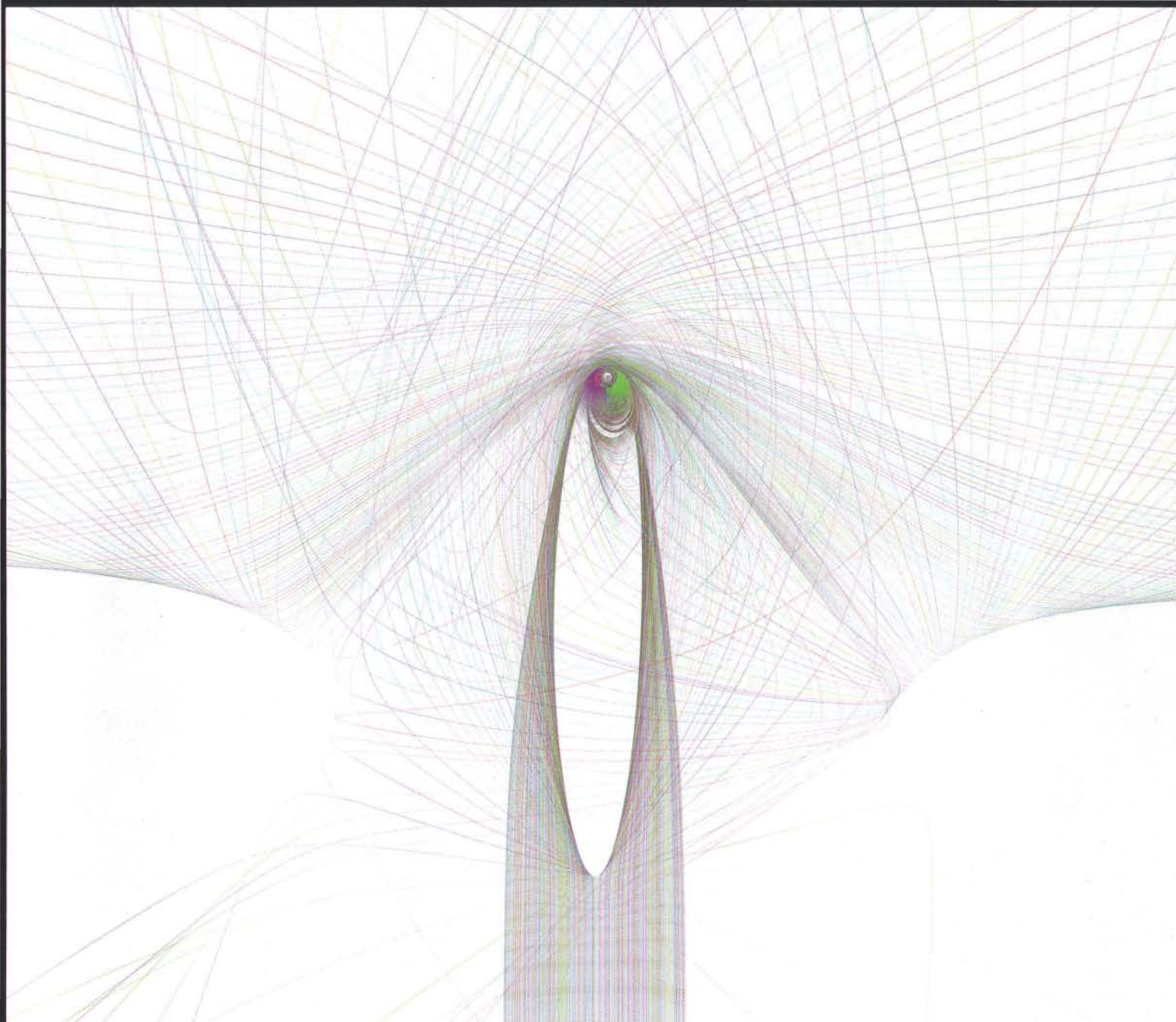
Canonical quantum gravity emerged in the 1950s and 1960s, when physicists rewrote Einstein's equations for gravity in the same form as the equations for electromagnetism, the idea being that the same techniques used to develop a quantum theory of electromagnetism could then be applied to gravity as well. When physicists John Wheeler and Bryce DeWitt attempted this procedure in the late 1960s, they arrived at a very strange result. The equation (dubbed the Wheeler-DeWitt equation) utterly lacked a time variable. The symbol  $t$  denoting time had simply vanished.

Thus ensued decades of consternation among physicists. How could time just disappear? In retrospect, this result was not entirely surprising. As I mentioned earlier, time had already

## DEFENDERS OF TIME'S FLOW

Not all physicists think the world is fundamentally timeless. One of the more intriguing alternative ideas is causal set theory, developed by Rafael Sorkin and David Rideout of the Perimeter Institute for Theoretical Physics in Ontario. It supposes that the world is a set of events, called a causet, which grows as new events come into existence according to probabilistic rules. The hope is that the process reproduces the features of spacetime that we perceive, including the flow of time. An outstanding question, though, is whether this process produces worlds that are compatible with relativity theory.





**RELATIONAL WORLD:** Time might have no independent existence but instead arise as a way to describe the relations among objects. This idea inspired Keith Peters to loop sets of lines around one another.

nearly disappeared from general relativity even before physicists attempted to merge it with quantum mechanics.

If you take this result literally, time does not really exist. Carlo Rovelli of the University of the Mediterranean in Marseille, France, one of the founders of loop quantum gravity, entitled his FQXi essay "Forget Time." He and English physicist Julian Barbour are the most prominent proponents of this idea. They have attempted to rewrite quantum mechanics in a timeless manner, as relativity appears to require.

The reason they think this maneuver is possible is that although general relativity lacks a global time, it still manages to describe change. In essence, it does so by relating physical systems directly to one another rather than to some abstract notion of global time. In Einstein's thought

experiments, observers establish the timing of events by comparing clocks using light signals. We might describe the variation in the location of a satellite around Earth in terms of the ticks of a clock in my kitchen, or vice versa. What we are doing is describing the correlations between two physical objects, minus any global time as intermediary. Instead of describing my hair color as changing with time, we can correlate it with the satellite's orbit. Instead of saying a baseball accelerates at 10 meters per second per second, we can describe it in terms of the change of a glacier. And so on. Time becomes redundant. Change can be described without it.

This vast network of correlations is neatly organized, so that we can define something called "time" and relate everything to it, relieving ourselves of the burden of keeping track of all those



direct relations. Physicists are able to compactly summarize the workings of the universe in terms of physical laws that play out in time. But this convenient fact should not trick us into thinking that time is a fundamental part of the world's furniture. Money, too, makes life much easier than negotiating a barter transaction every time you want to buy coffee. But it is an invented placeholder for the things we value, not something we value in and of itself. Similarly, time allows us to relate physical systems to one another without trying to figure out exactly how a glacier relates to a baseball. But it, too, is a convenient fiction that no more exists fundamentally in the natural world than money does.

Getting rid of time has its appeal but inflicts a good deal of collateral damage. For one, it requires quantum mechanics to be thoroughly rethought. Consider the famous case of Schrödinger's cat. The cat is suspended between life and death, its fate hinging on the state of a quantum particle. In the usual way of thinking, the cat becomes one or the other after a measurement or some equivalent process takes place. Rovelli, though, would argue that the status of the cat is never resolved. The poor thing may be dead with respect to itself, alive relative to a human in the room, dead relative to a second human outside the room, and so on.

It is one thing to make the timing of the cat's death depend on the observer, as special relativity does. It is rather more surprising to make whether it even happens relative, as Rovelli suggests, following the spirit of relativity as far as it will go. Because time is so basic, banishing it would transform physicists' worldview.

## The Recovery of Time

Even if the world is fundamentally timeless, still it seems as though it does have time in it. An urgent question for anyone espousing timeless quantum gravity is explaining why the world seems temporal. General relativity, too, lacks Newtonian time, but at least it has various partial substitutes that together behave like Newtonian time when gravity is weak and relative velocities low. The Wheeler-DeWitt equation lacks even those substitutes. Barbour and Rovelli have each offered suggestions for how time (or at least the illusion of time) could pop out of nothingness. But canonical quantum gravity already offers a more developed idea.

Known as semiclassical time, it goes back to a 1931 paper by English physicist Nevill F. Mott that described the collision between a helium nu-

cleus and a larger atom. To model the total system, Mott applied an equation that lacks time and usually is applied only to static systems. He then divided the system into two subsystems and used the helium nucleus as a "clock" for the atom. Remarkably, the atom, relative to the nucleus, obeys the standard time-dependent equation of quantum mechanics. A function of space plays the role of time. So even though the system as a whole is timeless, the individual pieces are not. Hidden in the timeless equation for the total system is a time for the subsystem.

Much the same works for quantum gravity, as Claus Kiefer of the University of Cologne in Germany, following in the footsteps of Thomas Banks of the University of California, Santa Cruz, and others, argued in his FQXi essay. The universe may be timeless, but if you imagine breaking it into pieces, some of the pieces can serve as clocks for the others. Time emerges from timelessness. We perceive time because we are, by our very nature, one of those pieces.

As interesting and startling as this idea is, it leaves us wanting more. The universe cannot always be broken up into pieces that serve as clocks, and in those cases, the theory makes no probabilistic predictions. Handling those situations will take a full quantum theory of gravity and a deeper rethinking of time.

Historically, physicists began with the highly structured time of experience, the time of a fixed past, present and open future. They gradually dismantled this structure, and little, if any, of it remains. Researchers must now reverse this train of thought and reconstruct the time of experience from the time of nonfundamental physics, which itself may need to be reconstructed from a network of correlations among pieces of a fundamental static world.

French philosopher Maurice Merleau-Ponty argued that time itself does not really flow and that its apparent flow is a product of our "sur-reptitiously putting into the river a witness of its course." That is, the tendency to believe time flows is a result of forgetting to put ourselves and our connections to the world into the picture. Merleau-Ponty was speaking of our subjective experience of time, and until recently no one ever guessed that objective time might itself be explained as a result of those connections. Time may exist only by breaking the world into subsystems and looking at what ties them together. In this picture, physical time emerges by virtue of our thinking ourselves as separate from everything else. ■

## MORE TO EXPLORE

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**From Eternity to Here: The Quest for the Ultimate Theory of Time.** Sean M. Carroll. Dutton, 2010.

**Does Time Exist in Quantum Gravity?** Claus Kiefer. [www.fqxi.org/community/forum/topic/265](http://www.fqxi.org/community/forum/topic/265)

**Forget Time.** Carlo Rovelli. [www.fqxi.org/community/forum/topic/237](http://www.fqxi.org/community/forum/topic/237)

**The Nature of Time.** Julian Barbour. [www.fqxi.org/community/forum/topic/360](http://www.fqxi.org/community/forum/topic/360)

**What Makes Time Special.** Craig Callender. [www.fqxi.org/community/forum/topic/302](http://www.fqxi.org/community/forum/topic/302)



# Washing

## CARBON OUT OF THE AIR

**Machines could absorb carbon dioxide from the atmosphere, slowing or even reversing its rise and reducing global warming**

**By Klaus S. Lackner**

**T**he world cannot afford to dump more carbon dioxide into the atmosphere. Yet it is not cutting back. All indications are that the concentration of CO<sub>2</sub> will continue to rise for decades. Despite great support for renewable energy, developed and developing countries will probably burn more oil, coal and natural gas in the future.

For transportation, the alternatives to petroleum appear especially far off. Onboard energy storage for electric vehicles is difficult; for a given mass, batteries hold less than 1 percent of the energy stored in gasoline. Carrying hydrogen on vehicles requires 10 times the storage volume of gasoline, and the high-pressure tank needed to hold it is very heavy. Although a few maiden flights of airplanes powered by jet fuel derived from biomass have taken place, it is unclear that biofuels can be produced at the quantities and

low prices required by airliners ... or by ships for that matter.

So how are we to keep the CO<sub>2</sub> concentration from rising beyond its current level of 389 parts per million? Unless we ban carbon-based fuels, one option is to pull CO<sub>2</sub> out of the air. Allowing forests to expand in area could absorb some of the gas, but humans produce so much that we simply do not have the land available to sequester enough of it. Fortunately, filtering machines—think of them as synthetic trees—can capture far more CO<sub>2</sub> than natural trees of a similar size.

Several research groups are studying prototype machines, among them the Georgia Institute of Technology, the University of Calgary in Canada, the Swiss Federal Institute of Technology in Zurich, and my own teams at Columbia University and Global Research Technologies in





Tucson, Ariz. [see “Competing Processes” on page 53]. All the designs involve variations on the same theme: as air breezes through a structure, it contacts a “sorbent” material that chemically binds the  $\text{CO}_2$ , leaving the nitrogen, oxygen and other elements to waft away.

Carbon dioxide would have to be captured on a grand scale to curtail climate change, but the basic concept is already well established. For decades scrubbers have removed  $\text{CO}_2$  from the air breathed inside submarines and spaceships and from air used to produce liquid nitrogen. Various chemical processes can accomplish this scrubbing, but machines with solid sorbents promise to trap the most gas per unit of energy required. Early, small prototype units suggest that wide dissemination of solid-sorbent machines could stop or even reverse the rise of atmospheric  $\text{CO}_2$ .

### One Big Filter

Like their leafy counterparts, air capture machines come in different shapes and sizes. Demonstration units intended to go beyond the laboratory prototypes should each trap from a ton to hundreds of tons of  $\text{CO}_2$  per day. The design being developed by Columbia and Global Research Technologies offers an example of how the technology can work. Thin fibers of sorbent material are arranged into large, flat panels akin to furnace filters, one meter wide and 2.5 meters high. The upright filter panels will revolve around a circular, horizontal track that is mounted on top of a standard 40-foot (12.2 meters) shipping container [see illustration on next page]. The panels will be exposed to the air. Once they are loaded with  $\text{CO}_2$ , they will move off the track and down into a regeneration chamber inside the container. There the

### KEY CONCEPTS

- Machines with filters made from sorbent materials can bind carbon dioxide, extracting it from the air.
- With mass production, machines might capture  $\text{CO}_2$  at \$30 a ton, less than the \$100 or more charged for commercial  $\text{CO}_2$  supply.
- With improved sorbents, 10 million machines across the planet could reduce  $\text{CO}_2$  concentration by five parts per million a year, more than the rate of global increase right now.

—The Editors

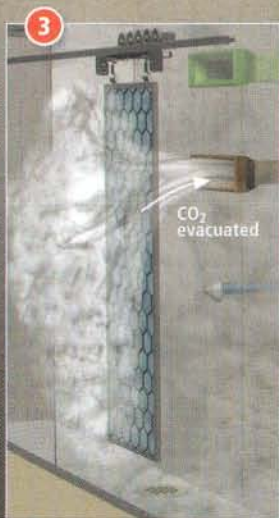
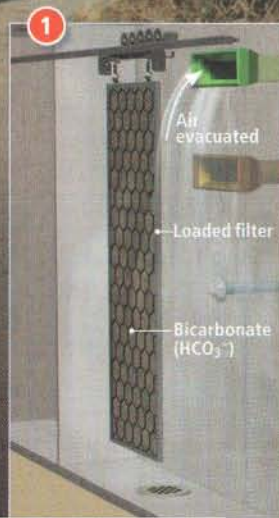
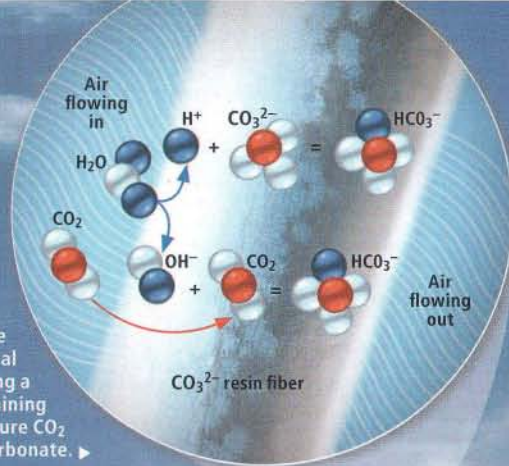


[MACHINE DESIGN]

# CARBON CAROUSEL

In a Global Research Technologies plan, air breezes through resin filters that slowly revolve around a track, absorbing  $\text{CO}_2$  (inset). An elevator unhooks a loaded filter and lowers it into a shipping container, where it is transferred to one of six regeneration chambers that extract the  $\text{CO}_2$  (bottom panels). The elevator then hangs the cleansed filter back on the track to begin trapping  $\text{CO}_2$  again.

Capture occurs when air wafts through fibers covered by negatively charged carbonate ions ( $\text{CO}_3^{2-}$ ), which attract the hydrogen ions ( $\text{H}^+$ ) from residual water molecules ( $\text{H}_2\text{O}$ ), forming a bicarbonate ( $\text{HCO}_3^-$ ). The remaining hydroxide ions ( $\text{OH}^-$ ) capture  $\text{CO}_2$  molecules, also forming bicarbonate.



Cleaning a filter begins by evacuating air from the chamber ①. Water is then sprayed to dissolve the bicarbonate on the fibers, which reverts to carbonate and  $\text{CO}_2$  ②. The  $\text{CO}_2$  is evacuated and compressed into a liquid, for storage or use by industry ③. Water is collected through a drain ④.



trapped gas will be freed from the sorbent and compressed to a liquid. The refreshed panel will be moved back up onto the track to pull more gas from the wind.

The CO<sub>2</sub> collected by air capture machines could be used profitably by industry or be piped underground, as is done in experimental carbon capture and storage systems, intended largely for use at coal-fired power plants. As an enticing alternative, however, the gas could serve as the feedstock for synthetic liquid fuels for transportation. Electricity would break one oxygen atom off a CO<sub>2</sub> molecule and one off a water molecule (H<sub>2</sub>O). The resulting mixture of CO and H<sub>2</sub> is known as synthesis gas, which, made by other means, has been used for almost a century as a feedstock for fuels and plastics. For years the South African energy company Sasol has been making synthetic gasoline and diesel with synthesis gas produced from coal. Air capture could therefore offset the emissions from vehicles that burn fossil fuels or help replace those fuels with synthetic liquids that do not require mining or drilling of coal, oil or natural gas.

Of course, air capture must not only work chemically; it must be practical, cost-effective and energy-efficient. To be practical, the equipment required to snatch CO<sub>2</sub> from the air would have to be compact. In one day more than 700 kilograms of CO<sub>2</sub> passes through a door-size opening, at ground level or altitude, that is exposed to a wind speed of six meters per second, common for a windmill site. That amount is equivalent to the CO<sub>2</sub> output of 13 people in the U.S. across the same period. Although air collectors might not see such high wind speeds, and the filtering will slow the flow, and even though trapping 100 percent of the gas is unlikely, the collectors would still be compact.

When assessing cost, two basic steps have to be considered: absorbing the CO<sub>2</sub> from the air and recovering the carbon from the sorbent. Based on a comparison with windmills, I concluded early on that the cost of filtering the air with a sorbent can be small. The subsequent act of liberating the CO<sub>2</sub> from the sorbent dominates the cost of the overall process. Nevertheless, air capture is still a significantly more practical alternative to scrubbing the tailpipes of millions of vehicles, because a large volume of CO<sub>2</sub> would have to be stored onboard each vehicle and returned to a collection point (every kilogram of gasoline burned by an engine produces three kilograms of CO<sub>2</sub>). Washing the ambient air is more viable.

## Wet Sorbent or Dry

From a chemist's point of view, a successful sorbent has to bind CO<sub>2</sub> strongly enough to absorb the gas but not hold it so strongly that subsequently freeing the gas for storage is expensive. The concentration in ambient air is about 0.04 percent, compared with 10 to 15 percent in a coal plant's flue gas. But the required strength of the sorbent varies only slightly with the carbon dioxide concentration, so sorbents for air capture can be similar in strength to those for flue-gas scrubbing.

Sorbents can be constructed as solids or liquids. Liquids are appealing because they can be transferred between collector and regenerator easily. Maintaining good surface exposure of a liquid to ambient air is challenging, but chemical engineering methods for this task are well understood. For example, David Keith, working at the University of Calgary and a new start-up company called Carbon Engineering, is using a sodium hydroxide solution that is trickled into a bed of plastic surfaces, through which air is blown by a fan. Moving the liquid is easy, but the strong binding of carbon dioxide to sodium hydroxide makes removal from the sorbent relatively difficult.

Solid sorbents are desirable because their surfaces can be roughened, creating more binding sites for CO<sub>2</sub> molecules, which raises uptake rates. Moving solid sorbents to and from a regeneration chamber is more difficult than it is for liquids, however. A commercial partnership called Global Thermostat, based on work at the Georgia Institute of Technology, is investigating solid sorbents that are heated to release the CO<sub>2</sub> they capture.

Both solid and liquid sorbents rely on acid-base chemistry. Carbon dioxide is an acid, and most sorbents are bases. They react with one another to form a salt. As an example, sodium hydroxide, known as caustic soda, is a powerful sorbent that binds carbon dioxide by forming sodium carbonate (soda ash). Sodium carbonate is still basic and can absorb additional carbon dioxide, transforming into sodium bicarbonate (baking soda), which is also a base. Similar chemistry occurs with other sorbents.

It should in principle be possible to remove CO<sub>2</sub> from a bicarbonate and return the sorbent to its hydroxide state, thereby continually recycling the sorbent. But in practice, regeneration methods seem to work well only for a half-step: they either remove carbon dioxide from a bicarbonate, resulting in a carbonate, or they remove

## PLANETARY PLAN

One vision for slowing global warming:

**10 million**  
air capture machines worldwide

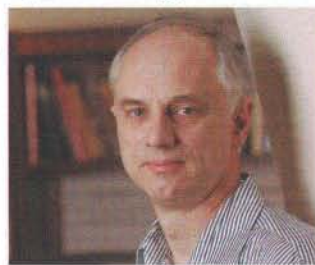
**10 tons**  
of CO<sub>2</sub> a day pulled from the air by each machine, after accounting for emissions related to energy consumed by the machines

**36 gigatons**  
a year of CO<sub>2</sub> captured overall

**5 parts per million**  
shaved annually from the CO<sub>2</sub> concentration in the earth's atmosphere, now at 389 ppm and rising

### [THE AUTHOR]

**Klaus S. Lackner**, a professor of geophysics, is chair of the department of earth and environmental engineering at Columbia University, where he is also a member of the Earth Institute. Lackner is co-founder of Global Research Technologies, a company that Gary Comer, the late owner of Lands' End, funded to demonstrate air capture technology.





## SELLING CO<sub>2</sub>

Carbon dioxide sucked from the air could be sequestered underground, or it could be sold as a processing agent or raw material for existing and future industries.

### EXISTING APPLICATIONS

- Pressurizing agent to force oil from enhanced oil recovery fields.
- Carbonation for beverages.
- Freezing agent for chicken wings.

### FUTURE APPLICATIONS

- Feedstock for synthetic gasoline.
- Nutrient for algae farms that produce biofuel.
- Raw material for carbonate-based cement.

carbon dioxide from a carbonate, resulting in a hydroxide. Cycling back and forth between bicarbonate and carbonate is preferable because less energy is required to free the CO<sub>2</sub> once it has bound to the sorbent.

Several classes of innovative sorbents can swing between carbonates and bicarbonates. One class comprises so-called anion exchange resins. These plasticlike carbonate polymers are employed in a variety of chemical processes, including the preparation of deionized water. The positive ions in the resin are fixed in place, and negative ions are mobile. One set of negative ions can be exchanged for another by washing the resin in a solution that offers different negative ions.

Global Research Technologies has devised one such carbonate resin. Filters made from dry resin and exposed to the wind load up with carbon dioxide until the resin reaches the bicarbonate state. Wetting the resin releases the captured carbon dioxide, and the resin reverts to carbonate. Once the resin dries, it can begin absorbing carbon dioxide again.

In our planned system, a loaded filter will descend into a regeneration chamber housed inside the shipping container. The air will be pumped out, and water, perhaps in the form of mist, will be added. The moist resin will release the CO<sub>2</sub>, which will be pumped out and compressed into a liquid. Compression also will force any residual water vapor to condense into pure water, which will be withdrawn and reused. The cleansed filter will rise back above the regeneration chamber to dry and then resume absorbing carbon dioxide above the shipping container.

Energy consumption by such machines is dominated by two steps. The first is pumping

the air out of the regeneration chamber. The second, which demands far more energy, is compressing the carbon dioxide from a fraction of an atmosphere to the pressure required to liquefy it (several tens of atmospheres, depending on temperature). The total process for collecting 1.0 kilogram of carbon dioxide from our design will require 1.1 megajoules of electricity. For comparison, when power plants across the U.S. are averaged, generating 1.1 megajoules of electricity produces 0.21 kilogram of carbon dioxide. Therefore, the air capture process collects far more carbon dioxide than it creates through energy consumption.

Realistic cost for the energy required is around \$15 per ton of carbon dioxide collected—not much greater than the cost of scrubbing the gas from a flue stack. Right now, however, most of the expense for deploying units would be in manufacturing and maintenance, costs that would decrease as production numbers rose. I expect the initial cost of air capture to be around \$200 per ton of carbon dioxide, with prices dropping dramatically as more collectors are built.

### Use It, Store It

Aside from being stored, what can be done with all the CO<sub>2</sub> that would be collected? Several options present themselves.

Many industries use carbon dioxide—to carbonate beverages, freeze chicken wings and make dry ice. The gas is also used for stimulating the growth of indoor crops and as a nonpolluting solvent or refrigerant. Few industrial sources exist, so the price is driven by the cost of shipping. In the U.S., CO<sub>2</sub> usually sells for more than \$100 a ton, but in remote locations the price can double or triple. The world market approaches 30 million tons annually, some of



OIL RECOVERY



ALGAE FARM



CEMENT



## [TERMINOLOGY]

# Not Geoengineering

Some people label the extraction of carbon dioxide from the air as geoengineering. I do not, because the process does not change the natural dynamics of the earth or create a potential environmental risk. Geoengineering schemes do: lofting aerosols into the upper atmosphere to absorb sunlight alters the chemistry of the atmosphere and the radiation balance across the globe. Spreading iron particles over the ocean surface to speed growth of algae that can absorb CO<sub>2</sub> alters the ocean's chemistry and biology. Air capture simply withdraws the excess CO<sub>2</sub> from the atmosphere that humans are putting there. —K.S.L.

which could be serviced by air capture units.

Niche markets such as food processing can provide a toehold. As more air capture units are made, prices will come down, increasing market size. Once the price of a ton of captured CO<sub>2</sub> has dropped well below \$100, extraction could also be sold as a carbon credit, like those traded on the Carbon Exchange in London.

Emerging markets could accelerate the technology's maturity. Since the 1970s petroleum companies have purchased CO<sub>2</sub> for enhanced recovery; the gas is pumped underground to force more oil or natural gas from dwindling fields. If the CO<sub>2</sub> came from air capture, the companies could claim a carbon credit for the gas that stays underground; typically about half of the injected gas stays there naturally. Enhanced oil recovery is a potentially large market, but many oil fields are far away from CO<sub>2</sub> sources. Installing capture units right above a field could change that dynamic.

With the advent of clean energy sources, however, the prize for air capture would be the production of fresh liquid fuel from CO<sub>2</sub> feedstock. As noted earlier, well-established technologies such as electrolysis and reverse water-gas shift reactions can produce synthesis gas from CO<sub>2</sub> and water, leading to fuel synthesis. The big cost is the electricity needed.

Until fuel synthesis becomes affordable, humankind will have to dispose of all the emissions it generates. Technologies such as geologic sequestration and mineral sequestration are being developed for storing CO<sub>2</sub> collected at power plants. Air capture can work with the same storage approaches, and machines could be installed at the same disposal sites.

## Global Cooling

Until clean transportation technologies become significantly more efficient, extracting carbon from the air would allow cars, planes and ships to continue burning liquid fuels, with their emissions captured by faraway air collectors. And "far away" is the case. Unlike ozone or sulfur dioxide, CO<sub>2</sub> remains in the atmosphere for decades to centuries, giving it ample time to travel extensively. The atmosphere mixes so thoroughly that it is legitimate to remove CO<sub>2</sub> from the air in Australia and take credit against emissions in North America. An equivalent amount of the gas could even be removed before emissions are released; a car could be made carbon-neutral by collecting its estimated lifetime emission of 100 tons before the vehicle rolls off the assembly line.

Air capture could also be a cheaper way to sequester emissions from power plants, especially older ones not easily retrofitted with flue-stack scrubbers or those located far from storage sites. And in a future world in which atmospheric CO<sub>2</sub> concentrations have already been stabilized, air capture could even drive levels down. In effect, air capture can deal with past emissions.

In addition to cost, critics argue that numerous air capture machines would consume lots of energy, and they note that the filters are made of plastics derived from oil. A more substantial hurdle, in my mind, is that for each ton of CO<sub>2</sub> collected, several tons of water would evaporate to the atmosphere, as wet filters dried. But if air capture were implemented on a large scale, it could start to correct climate change. Transportable units could collect about one ton apiece a day. Ten million such units could collect 3.6 gigatons a year, which would reduce atmospheric levels by about 0.5 ppm a year. If over time the units could handle 10 tons a day (which would require improved sorbents), the annual reduction would be 5 ppm a year, which is more than the rate of global increase right now. Note that even though 10 million units may seem large, the world produces about 71 million cars and light trucks every year.

Initially the cost to capture CO<sub>2</sub> would be high, about \$200 per ton as noted. If the technology follows standard learning and manufacturing curves, however, we could end up with costs that are dominated by materials and energy, which puts capture in the \$30 per ton range. At that point the cost added to a gallon of gasoline to pay for capturing the CO<sub>2</sub> it creates would be 25 cents—a price well worth paying. ■

## COMPETING PROCESSES

Various organizations are investigating dry and wet sorbents that could lead to commercial air capture machines. A sampling:

### DRY SORBENTS

Columbia University and Global Research Technologies: Carbonate polymer

Georgia Institute of Technology and Global Thermostat: Carbonate polymer

### WET SORBENTS

Brookhaven National Laboratory: Hydroxide solution

University of Calgary and Carbon Engineering: Hydroxide solution

Xerox PARC: Hydroxide solution

Swiss Federal Institute of Technology, Zurich: Hydroxide solution, lime

Paul Scherrer Institute: Hydroxide solution, lime

## ➔ MORE TO EXPLORE

Climate Strategy with CO<sub>2</sub> Capture from the Air. David W. Keith et al. in *Climatic Change*, Vol. 74, pages 17–45; January 2006.

Fixing Climate: What Past Climate Changes Reveal about the Current Threat—and How to Counter It. Wallace S. Broecker and Robert Kunzig. Hill and Wang, 2008.

Capture of Carbon Dioxide from Ambient Air. Klaus S. Lackner in *European Physical Journal: Special Topics*, Vol. 176, No. 1; pages 93–106; September 2009.



# Did Neandertals Think Like Us?

João Zilhão defends his controversial view that our oft-maligned relatives shared our cognitive abilities

## KEY CONCEPTS

- Scientists have traditionally considered *Homo sapiens* the only species to invent and use symbols.
- But over the past few decades archaeologists have discovered a handful of enigmatic artifacts hinting that our cousins the Neandertals—long dismissed as intellectually inferior—might have engaged in symbolic activities, too. Experts dismissed the finds, however, attributing them to modern humans instead.
- The recent discovery of Neandertal jewelry and body paint from two sites in Spain provides unequivocal evidence of Neandertal symbolism and suggests that modern human behavior has ancient roots.

—The Editors

For the past two decades archaeologist João Zilhão of the University of Bristol in England has been studying our closest cousins, the Neandertals, who occupied Eurasia for more than 200,000 years before mysteriously disappearing some 28,000 years ago. Experts in this field have long debated just how similar Neandertal cognition was to our own. Occupying center stage in this controversy are a handful of Neandertal sites that contain cultural remains indicative of symbol use—including jewelry—a defining element of modern human behavior. Zilhão and others argue that Neandertals invented these symbolic traditions on their own, before anatomically modern humans arrived in Europe around 40,000 years ago. Critics, however, believe the items originated with moderns.

But this past January, in a paper published in the *Proceedings of the National Academy of Sciences USA*, Zilhão and his colleagues reported on finds that could settle the dispute: pigment-stained seashells from two sites in Spain dated to nearly 50,000 years ago—10,000 years before anatomically modern humans made their way to Europe. Zilhão recently discussed the implications of his team's new discoveries with *Scientific American* staff editor Kate Wong. An edited version of their conversation follows.

**SCIENTIFIC AMERICAN:** Paleoanthropologists have been arguing about Neandertal behavior for decades. Why all the fuss?

**JOÃO ZILHÃO:** The debate of the past 25 years stems from the theory that anatomically modern humans originated in Africa as a new species and then spread out from there, replacing archaic humans such as the Neandertals. Added to this notion was the tenet that species are defined as much by anatomy as by behavior. Thus, Neandertals, not being modern in anatomy, could not by definition be modern in behavior.

But there were problems with this model. In 1979 archaeologists working at the site of St. Césaire in France found a Neandertal skeleton in a layer containing cultural remains made in the so-called Châtelperronian tradition. At the time, experts believed that the Châtelperronian artifacts—body ornaments and sophisticated bone tools, among other elements—were manufactured by modern humans. But the St. Césaire find established its association with the Neandertals instead. Then, in 1995, researchers determined that the human remains found in the Châtelperronian levels of another French site, the Grotte du Renne at Arcy-sur-Cure, were also those of Neandertals.

To reconcile these discoveries with the idea





that modern humans alone were capable of such advanced practices, some researchers proposed that the artifacts somehow got mixed into the Neandertal deposits from overlying early-modern human deposits. Others argued that the Neandertals simply copied their modern human contemporaries or obtained the items from them through scavenging or trade but did not really understand them and never integrated them into their culture in the same way moderns did. This controversy has never really been settled to the satisfaction of all those involved, which is where our new finds from Spain come in.

**SA:** What exactly did you find and how did you find it?

**JZ:** The material comes from two sites. One is a cave in southeast Spain called Cueva de los Aviones, which was excavated in 1985 by Ricardo Montes-Bernárdez of the Fundación de Estudios Murcianos Marqués de Corvera. In his reports Montes-Bernárdez mentioned having found three perforated cockle shells in the deposits, but no one paid attention at the time. After reading about the shells in his papers a few years ago, I went to the museum housing the materials he

▲ **NEANDERTAL ADORNMENTS** appear to have included face paint and pendants, according to recent discoveries made at two sites in Spain. Such items indicate that Neandertals were capable of symbolic thought—a crucial element of modern human behavior.



collected and asked to see them. They immediately struck me as being of major importance because such shells are typically considered pendants when discovered in archaeological deposits. But we didn't know the age of the material, so the first thing was to select samples for radiocarbon dating. The dates came out at 48,000 to 50,000 years ago.

Because most of the shells in the collection had never been washed, I checked to see if there were other specimens of note. One of the shells turned out to be a Mediterranean oyster shell, the cleaning of which revealed a stain that I thought could be pigment residue. Analysis of the substance identified it as a mix of red pigment, called lepidocrocite, and finely ground up bits of dark red and black hematite and pyrite, which would have added sparkle. My colleagues and I also came across a naturally pointed horse bone bearing some reddish pigment on the tip. And we found lumps of yellow and red pigment, including a very large deposit of a mineral called natrojarosite, the quantity and purity of which indicated that it had been stored in a purse that eventually perished, leaving only the mineral behind.

**SA:** What did you unearth at the second site?

**JZ:** At around the same time that I was inspecting the Aviones collection, I was also going through the finds of the September 2008 field season at a large rock shelter some 60 kilometers inland from Aviones called Cueva Antón, where I have been excavating Neandertal deposits since 2006. One of the items was a perforated scallop shell that one of my undergraduate students had collected on the second day of excavation. I had originally thought it was a fossil shell unrelated to human activities. But when I started to clean it, I found it was very fresh and full of color. On closer inspection, it seemed that the whitish exterior of the shell had been painted with an orange pigment, which turned out to be a mix of hematite and another mineral called goethite.

**SA:** What do you think the Neandertals were doing with these items?

**JZ:** The interesting thing about natrojarosite is that it has only one known use, and that's as a cosmetic. So we infer that that's how it was used at Aviones as well. The horse bone with the reddish tip may have been used to mix or apply pigment or to pierce through hide that had been colored with pigment. And the unperforated Mediterranean oyster shell bearing the traces of a glittery red mixture was probably a paint cup.

The simplest explanation for the natrojarosite and sparkly red pigment and the context in which they were found is some kind of body painting, specifically facial painting. But whether the Neandertals applied them on a daily basis after waking up or whether it was something that they did for ritual reasons on special occasions—for celebrations or perhaps for mourning—we don't know.

In addition, one of the perforated cockle shells from Aviones had bits of red ochre adhering to its inner side near the hole. In this case, the most likely scenario is that the shell had been painted, because you cannot use a shell with holes in it as a container. Thus, in addition to painting their bodies, the Neandertals at both sites painted perforated shells, which they presumably used as pendants.

▼ **SCALLOP SHELL PENDANT** was painted with an orange pigment, perhaps so that the exterior of the shell (*right half*) matched the naturally colorful interior (*left half*). Pigment found on the tip of a naturally pointed horse foot bone (*above shell*) suggests that the Neandertals used the bone to mix or apply their paints.





**SA:** Your analyses did not yield evidence that the holes in the cockle and scallop shells at these sites were man-made, nor were you able to find traces of use on the edges of the holes themselves, so how do you know they were used decoratively?

**JZ:** These species are found only in deep water, so by the time they wash ashore they no longer contain any flesh, which means they were not collected for food. And they have pigments associated with them. What is the alternative? If you open any book of ethnographic shell ornaments from Africa or Oceania, you'll see examples of shells of these or related species with natural perforations used as ornaments.

**SA:** What are the implications of these discoveries in terms of understanding the origin of behavioral modernity in humans?

**JZ:** The one thing these finds make clear is that Neandertals were behaviorally modern. They were not like early modern humans anatomically, but they were cognitively as advanced or more so. There are several possible conclusions one could draw from this observation. Either modern cognition and modern behavior emerged independently in two different lineages, or they existed in the common ancestor of Neandertals and anatomically modern humans; or the groups we call Neandertals and modern humans were not different species and therefore we should not be surprised that despite the anatomical differences there are no cognitive differences, which is the conclusion I favor.

In my view, the emergence of modern human behavior is the slow, perhaps intermittent accumulation of knowledge that, as population densities increase, gives rise to social identification systems, which appear in the archaeological record in the form of personal ornaments, body painting, etcetera. That such early examples of behavioral modernity are rare is what we should expect. That's what the beginning of an exponential process like this one should look like.

**SA:** So modern behavior—as represented by body decoration, artwork, and so on—is the product of needing to communicate with or identify members of a growing population?

**JZ:** Yes, in a world where the frequency of encounters with strangers would be such that you need to have ways to know whether a stranger is



friend or foe, whether it's someone to whom your kin owes favors or is owed favors.

**SA:** But do you think something had to change in the hardware, the brain, at some point in the human lineage before modern human behavior could arise?

**JZ:** Yes, I think that happened 1.5 million to two million years ago—or somewhere between 500,000 and a million years ago at the latest—when average brain size reached the modern range. If we could clone a human who lived 500,000 years ago, put him in a surrogate womb, and then after birth nurture him as a human of today, would he be able to fly an airplane? Maybe some of my colleagues would say no, but my answer is he would.

**SA:** If Neandertals in Spain were making ornaments 10,000 years before moderns arrived in Europe, do you think that, rather than Neandertals copying moderns, the reverse might have occurred?

**JZ:** Prior to entering Europe, modern humans did not have pierced or grooved mammal teeth like the ones found in the Châtelperronian, nor did they have perforated bivalve shells like the ones we found in Spain. But once they enter Europe, they have them. Where did the moderns get these ornaments? If we were talking about people in the Copper Age, we would conclude that the incomers got them from the locals. Why should we have a different logic for Neandertal things?

▲ **JOÃO ZILHÃO** has long argued that Neandertals invented symbolic practices independently of anatomically modern humans. Here he sifts through sediments at a site located in the same region as the sites that yielded the Neandertal finds.

## ➔ MORE TO EXPLORE

**The Morning of the Modern Mind.** Kate Wong in *Scientific American*, Vol. 292, No. 6, pages 64–72; June 2005.

**Twilight of the Neandertals.** Kate Wong in *Scientific American*, Vol. 301, No. 2; pages 34–39; August 2009.

**Symbolic Use of Marine Shells and Mineral Pigments by Iberian Neandertals.** João Zilhão et al. in *Proceedings of the National Academy of Sciences USA*, Vol. 107, No. 3, pages 1023–1028; January 19, 2010.



# The Earth's Missing Ingredient

The discovery of a novel high-density mineral means that the earth's mantle is a more restless place than scientists suspected—and offers new clues to the planet's history • By Kei Hirose

## KEY CONCEPTS

- At high pressures, the most common type of mineral in the earth's lower mantle undergoes a structural change and becomes denser.
- The existence of this denser phase implies that the mantle is more dynamic and carries heat more efficiently than previously thought.
- Faster heat transport helps to explain why continents grew as fast as they did and even how the earth's magnetic field evolved in a way that enabled life to move onto land.

—The Editors

The deepest hole humans have ever dug reaches 12 kilometers below the ground of Russia's Kola Peninsula. Although we now have a spacecraft on its way to Pluto—about six billion kilometers away from the sun—we still cannot send a probe into the deep earth. For practical purposes, then, the center of the planet, which lies 6,380 kilometers below us, is farther away than the edge of our solar system. In fact, Pluto was discovered in 1930, and the existence of the earth's inner core was not established—using seismological data—until six years later.

Still, earth scientists have gained a surprising amount of insight about our planet. We know it is roughly structured like an onion, with the core, mantle and crust forming concentric layers. The mantle constitutes about 85 percent of the earth's volume, and its slow stirring drives the geologic cataclysms of the crust. This middle domain is mainly a mix of silicon, iron, oxygen, magnesium—each of which appears in roughly the same concentrations throughout the mantle—plus smaller amounts of other elements. But depending on the depth, these elements combine into different types of minerals. Thus, the mantle is itself divided into concentric layers, with different minerals predominating at different depths.

Although the nature and composition of most of those layers have been fairly well understood for decades, until recently the lowermost layer remained a bit of a puzzle. But in 2002 the synthesis in my laboratory of a novel, dense mineral that forms at the temperatures and pressures of the bottom 300 kilometers of the mantle solved the mystery. Since then, studies have revealed that the mineral, called postperovskite, dramatically af-



KEITH KASNOT







[THE NEW PICTURE]

# A More Complex Planet

The earth is structured like an onion, with different materials appearing in each concentric layer. The discovery of a new, high-density material, called postperovskite, implies the existence of a new layer of that onion and explains puzzling behavior by seismic waves traveling through the planet.

## CRUST (UP TO 35 KILOMETERS OF DEPTH)

The continents, which are in part submerged by the oceans, are made of diverse rock that is up to several billion years old and relatively light. Thus, they float on the denser mantle underneath. The heavy basaltic rock that forms the bulk of the oceanic crust originates from mantle magma that erupts at underwater ridges and eventually sinks back into the mantle, typically within 100 million years.

## MANTLE

Mantle rock consists primarily of oxygen, silicon and magnesium. Despite being mostly solid, it does deform on geologic timescales. In fact, the rock slowly flows as convective currents stir the entire mantle. That flow dissipates the earth's inner heat and propels continental drift.

### UPPER MANTLE (35–660 KM)

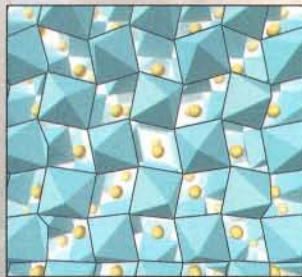
As greater depths bring higher pressures and temperatures, the mantle's elemental components arrange into different crystal structures (minerals), forming layers. Three minerals—olivine, modified spinel and spinel—give the layers of the upper mantle their respective names.

### LOWER MANTLE (660–2,900 KM)

The lower mantle was for decades thought to be relatively uniform in structure. But seismological data suggested that something different was happening at the bottom.

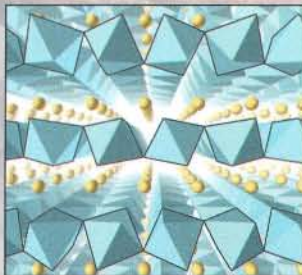
#### • Perovskite layer

The most prevalent mineral here (70 percent by weight) is a magnesium silicate ( $\text{MgSiO}_3$ ) belonging to the family of crystal structures called perovskites. In this densely packed structure, magnesium ions (yellow) are surrounded by octahedral silicon-oxygen groups (blue double-pyramid shapes). Until recently, scientists thought that no denser crystal arrangement of these elements could exist.



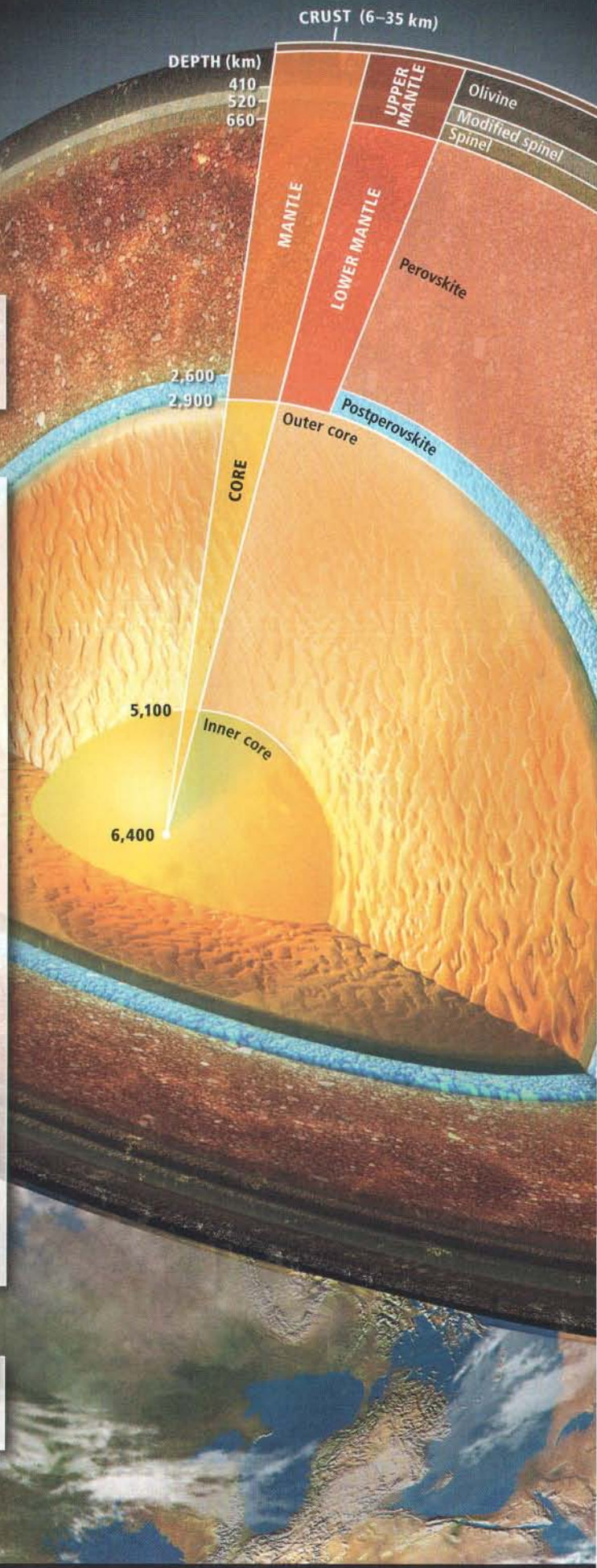
#### • Postperovskite layer

At the pressures and temperatures of the bottom 300 km of the mantle, perovskite transforms into a new structure: the magnesium ions and the silicon-oxygen groups arrange themselves into separate layers. The transition releases heat and reduces volume by roughly 1.5 percent—a small difference, but one with dramatic effects on the entire planet [see illustrations on pages 64–65].



## CORE (2,900–6,400 KM)

The deepest part of the earth consists predominantly of iron, which is liquid in the outer core and solid in the inner core. Convection stirs the outer core just as it stirs the mantle, but because the core is much denser, little mixing occurs between the mantle and the core. Core convection is thought to produce the planet's magnetic field.





fects the planet's dynamics. Its apparent presence in the mantle, researchers have shown, implies that the mantle's convection currents (in which cooler rock sinks and hotter rock upwells, taking some of the earth's inner heat with it) are more dynamic and more efficient at carrying heat than was thought. Without postperovskite, continents would have grown slower and volcanoes would have been quieter. The formation of postperovskite may also have hastened the strengthening of the earth's magnetic field, which made life possible on land by shielding it from cosmic rays and solar wind. In other words, postperovskite was a key missing ingredient for understanding the evolution of our planet.

### Rock Bottom

Geophysicists map the structure of the earth by measuring seismic waves. After an earthquake, because waves travel through the entire planet, sensitive instruments can pick them up on the other side of the world. When waves cross the boundaries between different materials, they may be refracted or reflected. Global measurements of such behavior have shown that the mantle has five layers, with each boundary between the layers marked by a jump in the waves' velocity. Researchers have linked these jumps to changes in the structure of the rock—changes attributed to the pressures and temperatures that exist as one goes deeper down.

Rock is made of different minerals. A mineral is an arrangement of atoms into a particular geometric pattern, or crystal, and thus has its own composition, physical properties and even color—think of the different types of grains in an ordinary granite kitchen counter. Below certain thresholds of depth down in the mantle, the enormous pressures and temperatures force the elements to rearrange into new crystal structures. As physicists say, the materials undergo a phase transition.

Lacking the ability to probe the depths of the earth, early geologists who wanted to study these structures had to look for mantle rocks to be brought up to the surface by magmas of deep

origin. These rocks often enclose diamonds. Because diamonds form under the pressures and temperatures that exist at 150 kilometers of depth or more, their host rocks can be presumed to originate from a similar depth; they thus provide a wealth of information about the uppermost part of the mantle. But mantle rocks or minerals derived from depths greater than 200 kilometers reach the surface only rarely.

As researchers learned to generate high pressures and temperatures in the laboratory, they became able to synthesize the minerals believed to make up lower levels of the mantle. The predominant minerals in the rock give the mantle's layers their names: in the upper mantle, those are the olivine, modified spinel and spinel layers. Then, starting at a depth of 660 kilometers, a dense form of magnesium silicate ( $\text{MgSiO}_3$ ) becomes the main component of the rock. It belongs to a vast family of crystals called perovskites, which are arrangements of negatively charged oxygen ions and two types of positively charged ions—in this case magnesium and silicon—held together by electrostatic attraction. Perovskites can have a wide variety of chemical compositions and include superconductors as well as materials widely used in electronics, for example, in piezoelectric actuators or in capacitors.

Magnesium silicate perovskite was first synthesized in 1974 under 30 gigapascals of pressure. (One gigapascal, or one billion pascals, is about equivalent to 10,000 times atmospheric pressure at sea level.) In the following 30 years the consensus among experts was that this mineral should be present all the way down to the bottom of the mantle, located at a depth of 2,890 kilometers, without undergoing another phase transition.

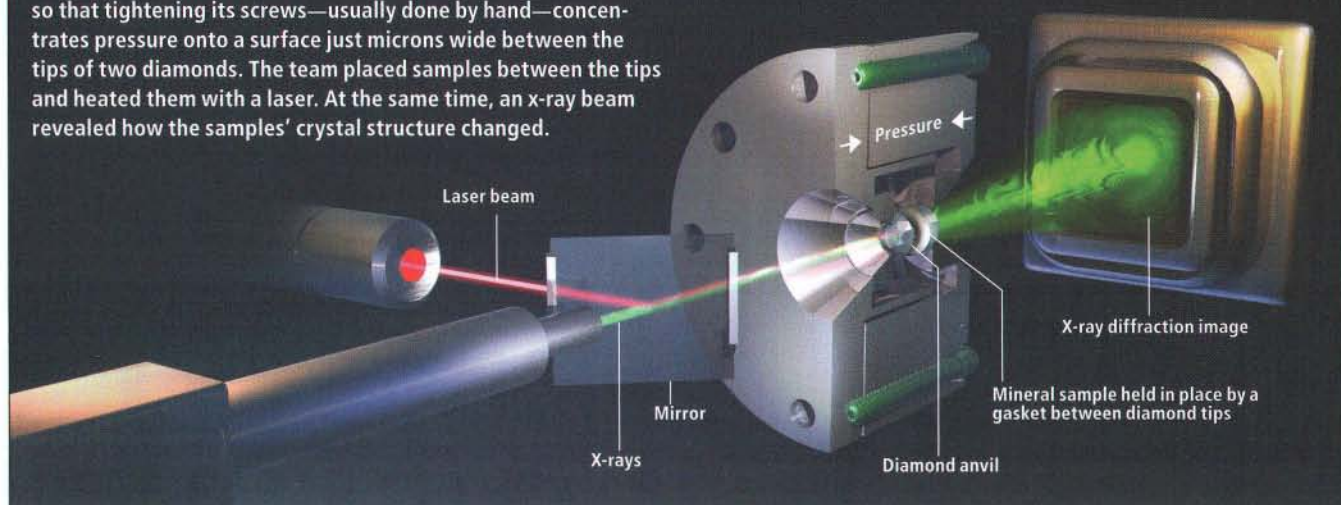
In the 1960s, however, a new seismic anomaly was found, around 2,600 kilometers down. The lower mantle, which used to be called the D-layer, was now divided into two sublayers, D' and D'' (D-prime and D-double-prime), with the D'' region occupying the bottom 300 kilometers or so of the shell. In 1983 the anomaly was found to be an actual discontinuity, but it was attributed to a change in the relative abundances of the elements, not to a phase-transition boundary. This assumption was made in part because perovskite is an "ideal" crystal structure—one in which the atoms are arranged in a tightly packed geometry that seems to maximize the mass per unit volume. Experts doubted that perovskite could be compressed into any structure with tighter packing than that. On the other hand, a change in the element abundances



[THE DISCOVERY]

# DEEP EARTH IN THE LAB

The author's team re-created the conditions of the lower mantle using a diamond-anvil cell. The cylindrical steel cell is designed so that tightening its screws—usually done by hand—concentrates pressure onto a surface just microns wide between the tips of two diamonds. The team placed samples between the tips and heated them with a laser. At the same time, an x-ray beam revealed how the samples' crystal structure changed.



was also problematic, because convection should stir up the lower mantle and mix its contents with those of the overlying layers, leading to uniformity in the kinds and ratios of elements.

To clarify the situation, experiments would need to push above 120 gigapascals and 2,500 kelvins. I got interested in this problem in the mid-1990s and later started laboratory experiments using a diamond-anvil cell, in which samples of mantlelike materials are squeezed to high pressure between a couple of gem-quality natural diamonds (about two tenths of a carat in size) and then heated with a laser. Above 80 gigapascals, even diamond—the hardest known material—starts to deform dramatically. To push pressure even higher, one needs to optimize the shape of the diamond anvil's tips so that the diamond will not break. My colleagues and I suffered numerous diamond failures, which cost not only research funds but sometimes our enthusiasm as well. Finally, by using beveled anvils, we broke the 120-gigapascal ceiling in 2001. We were one of the first labs in the world to do so and the first to study the effects of such pressures on perovskite.

## Crystal Clear

To understand what went on inside our samples, we set up our experiment at SPring-8, the world's largest synchrotron x-ray facility, located in the mountains of western Japan. For nearly a century scientists have decoded the structure of crystals by looking at how x-rays diffract through them (based on the fact that interatomic distances

are in the same range of lengths as the wavelengths of x-rays). SPring-8's hair-thin, intense beams of x-rays enabled us to take high-quality shots at intervals of just one second, which is quite useful for monitoring the change in crystal structure in such extreme conditions.

In the winter of 2002 at SPring-8, my student Motohiko Murakami came to me saying that the diffraction pattern of magnesium silicate perovskite had drastically changed when it was heated at 125 gigapascals. Such an observation usually points to a change in crystal structure—precisely what I had been looking for. If true, this discovery was going to be the most important in high-pressure mineralogy—and possibly in all of deep-earth science—since 1974, when silicate perovskite itself was first synthesized.

Nevertheless, at first I did not take these data too seriously, because diffraction patterns can change for any number of reasons. For example, samples can react chemically with the materials that hold them in the anvil—typically clay—resulting in a radical change in the diffraction data. When I told my close colleagues about this new observation several days later, their first reaction was rather negative. “You must be doing something wrong,” a crystallographer told me: perovskite is an ideal, tightly packed structure, he noted, and no phase transformation from perovskite into a denser structure had ever been seen before.

We repeated the experiments many times. Encouragingly, we observed the new diffraction pattern each time. We also found that when we

[THE AUTHOR]



**Kei Hirose** is professor of high-pressure earth sciences at the Tokyo Institute of Technology. He chose to major in geology at the University of Tokyo in the hope that the line of work would take him to Antarctica or allow him to explore the deep sea in a submersible. His research focuses on the generation of ultrahigh pressures and temperatures in laboratory experiments—with a special interest in deep-earth and planetary materials—but he has not yet given up his travel dreams.

ALFRED T. KAWAJIAN (top illustration); COURTESY OF KEI HIROSE (Hirose)



reheated the sample at low pressure the new pattern changed back to that of perovskite. Thus, the transition was reversible, which ruled out a change in the sample's chemical composition. At that point, I became convinced that we had transformed magnesium silicate perovskite into a new structure.

Next, we found that at a temperature of 2,500 kelvins, the transition happens at 120 (rather than 125) gigapascals—precisely the pressure corresponding to 2,600 kilometers of depth, where the mysterious discontinuity jump in seismic-wave velocity was found. I realized that the long-standing enigma had now been settled: we had discovered a new phase transition and a new material which must be predominant in the D'' layer. Furthermore, I speculated that the properties of the new phase might have important consequences for the dynamics of the mantle.

But before continuing our work, we first needed to determine the crystal structure of the new phase, which was challenging because at the time no perovskite-type crystals were known to transform into other crystals under pressure. For almost a year we scoured crystallography catalogues trying to fit our diffraction data to known patterns—a needle-in-a-haystack search, given that there are tens of thousands of such crystal structures. Then, at the end of 2003, during the New Year's holidays, my colleague Katsuyuki Kawamura, a chemist, ran a computer simulation of magnesium, silicon and oxygen atoms at high pressure. He started out with randomly distributed atoms at a very high temperature, and as he cooled his virtual sample, the mix began to crystallize. He then calculated the diffraction patterns such a crystal structure would produce, and the result perfectly matched the pattern we had observed experimentally.

We decided to name the new phase postperovskite. (Strictly speaking, it is not a mineral, because it has yet to be found in nature.) As it turns out, its structure is essentially identical to that of two known crystals, uranium ferrous sulfate ( $\text{UFeS}_3$ ) and calcium iridate ( $\text{CaIrO}_3$ ), which are stable under ambient conditions. And our direct measurements have shown that the density of postperovskite is indeed higher than that of perovskite, by 1 to 1.5 percent.

### Taking the Heat

Since we announced our results in 2004, researchers in various fields have built on them to craft an exciting new picture of the many different processes within the earth. To begin with,

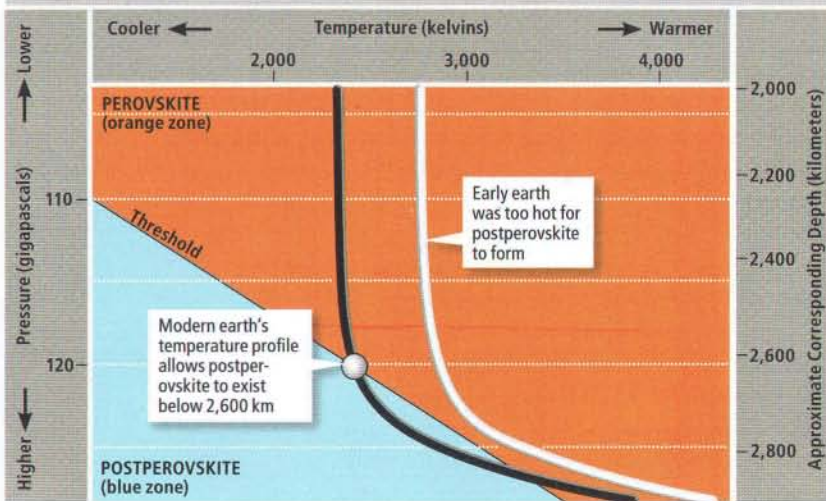
our discovery cast light on the amount of heat flowing from the core to the mantle. The core is mostly iron, making it twice as dense as the mantle. As a consequence, virtually no mixing occurs at the boundary between the two, and heat is exchanged predominantly by conduction. Whereas the mantle is rich in radioactive uranium, thorium and potassium, the core is probably poor in radioactive isotopes, which implies that its current temperature of perhaps 4,000 to 5,000 kelvins derives mostly from heat left over from the formation of the earth. Since then, the core has cooled with time as heat has transferred into the mantle at the core-mantle boundary.

By making plausible assumptions about the heat conductivities of the materials in the lower mantle, my collaborators and I were able to estimate that the rate at which heat flows from the core into the mantle may be five to 10 terawatts, comparable to the average output of all the world's power stations combined. It is a larger flow of energy, and hence a faster rate of core cooling, than previously thought. To be at its current temperature, then, the core must have started out at a higher temperature than had been assumed.

That flow of heat has determined how the core evolved since the earth formed. Inside the young earth, the core was entirely liquid, but at some point in the planet's history the inner core started to crystallize, so that it now has two layers: an inner, solid core and an outer, liquid core. The faster rate of cooling suggests that the solid

**Experts doubted that a mantle mineral could be compressed into a crystal structure with any tighter packing.**

EXPERIMENTAL DATA revealing the temperatures and pressures at which perovskite converts to postperovskite (*threshold line*) indicate that the earth's current range of temperatures (*black curve*) is just right for postperovskite to exist in the lowermost mantle, between about 2,600 and 2900 km of depth. In contrast, the early earth (*white curve*) was too hot to allow postperovskite's formation.



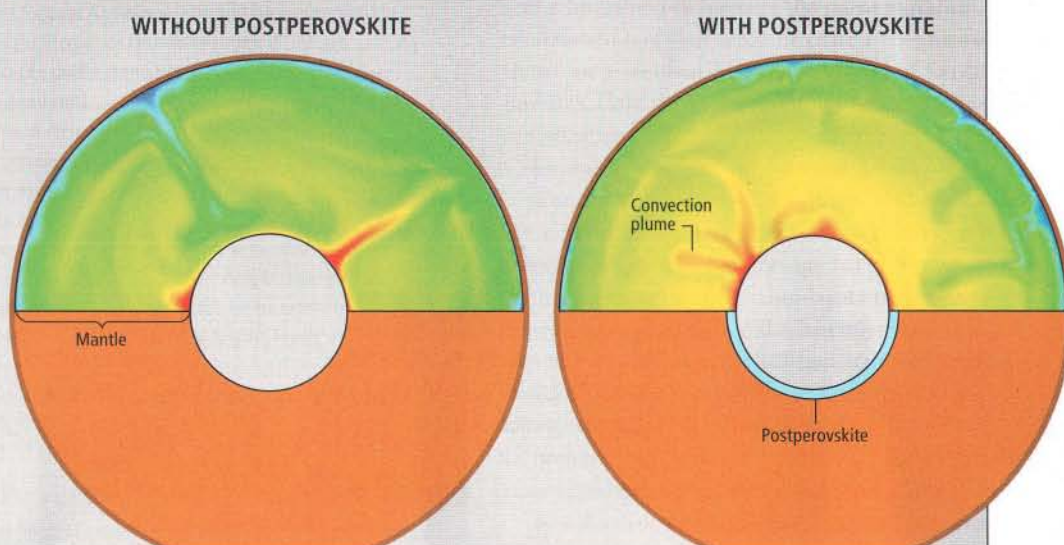


## [COMPUTER SIMULATIONS]

## CONVECTION ON STEROIDS

Simulations have shown that in the presence of postperovskite, convection is faster and more chaotic (right) than if the mantle contained only perovskite (left), as it did in the early earth. Convection plumes rise over the hot core, just like plumes of air form over hot ground. As a plume ascends, the postperovskite in it encounters lower pressures, causing it to transform into perovskite, which is less dense. The resulting expansion adds buoyancy to the plume, causing it to rise up faster and more chaotically than if the mantle contained only perovskite.

Cool Hot



inner core may be less than a billion years old, which is young compared with the earth's age of 4.6 billion years: otherwise the inner core would be much larger than we observe at present.

The formation of the inner core has implications for geomagnetism, which, in turn, has implications for life. Earth scientists believe that convection of liquid metal in the molten outer core is what generates the planet's magnetic field, by a dynamo action. The presence of a solid inner core makes the convection more regular and less chaotic, resulting in a stronger magnetic field than would exist if the core were entirely liquid. The geomagnetic field shields the earth from solar wind and cosmic rays, which can cause genetic mutations and would be especially dangerous for life on land. The change in the intensity of the geomagnetic field possibly around one billion years ago may thus have made it possible for life to expand from the seas onto dry land.

Postperovskite affects heat diffusion not just at the boundary between core and mantle but throughout the mantle as well, a discovery that has yielded further revelations about the earth's history. Mantle plumes form above the core-mantle boundary. As a plume ascends within the postperovskite layer, it encounters lower pressures, until a threshold is reached where the hot postperovskite transforms into less dense perovskite, which increases volume. Being less dense than the cooler material around it, the plume becomes still more buoyant, which promotes further upwelling. Computer simulations have shown that in the presence of postperovskite,

plumes form more often and meander more than if all of the lower mantle were simply made of perovskite [see box above]. The simulations have shown that, in this way, the advent of postperovskite probably sped up heat flow through the mantle by 20 percent.

### Causing a Stir

By speeding up mantle convection, the presence of postperovskite increases the temperature of the upper mantle by hundreds of degrees. One of the consequences is that volcanoes are more active than they would otherwise be. In the early earth, when the core was hotter, the lowermost part of the mantle was also hotter and outside the range of temperatures at which postperovskite can form. Paradoxically, though, without postperovskite to speed up heat flows, the upper mantle would have been cooler than it is now. As the planet slowly cooled, some perovskite started to turn into postperovskite, probably some 2.3 billion years ago, boosting the heat flow from the core and raising temperatures in the entire mantle. As a consequence, researchers have estimated, faster plate motion and increased volcanism may have led the continents to grow twice as fast during the past 2.3 billion years than they did during most of the previous time—although this conclusion is still being vigorously debated.

The physical properties of the D" layer may be remarkably different from those of the overlying mantle. Recent measurements have revealed that postperovskite has much higher electrical conductivity than perovskite, making the lowermost mantle more conductive by several

### MORE TO EXPLORE

**Perovskites.** Robert M. Hazen in *Scientific American*, Vol. 258, No. 6, pages 52–59; June 1988.

**Sculpting the Earth from Inside Out.** Michael Gurnis in *Scientific American*, Vol. 284, No. 3, pages 34–41; March 2001.

**Post-Perovskite Phase Transition in MgSiO<sub>3</sub>.** Motohiko Murakami, Kei Hirose, Katsuyuki Kawamura, Nagayoshi Sata and Yasuo Ohishi in *Science*, Vol. 304, pages 855–858; May 7, 2004.

**Deep Earth and Mineral Physics.** Special issue of *Elements*, Vol. 4, No. 3; June, 2008.

**Deep Mantle Properties.** Kei Hirose in *Science*, Vol. 327, pages 151–152; January 8, 2010.

FROM "EFFECTS OF A PEROVSKITE-POST PEROVSKITE PHASE CHANGE NEAR CORE-MANTLE BOUNDARY IN COMPRESSIBLE MANTLE CONVECTION," BY T. NAKAGAWA AND P. J. TACKLEY, IN *GEOPHYSICAL RESEARCH LETTERS*, VOL. 31, 2004



orders of magnitude. A highly conductive postperovskite layer would enhance the exchange of angular momentum between the liquid core and solid mantle whenever the core's flow-pattern changes. (The exchange results from what is called the Lorentz force.) According to simulations done by other researchers, this exchange would alter the earth's rotational speed in a way that closely agrees with millisecond variations that are actually observed in the length of the day on decadal time scales. The electric conductance of postperovskite and the resulting large exchange of angular momentum could also help explain the periodic precession of the earth's axis of rotation (nutation).

Although postperovskite is present only in the bottom few hundred kilometers of the earth's mantle, it could make up larger portions of other planets. Theory predicts that  $\text{MgSiO}_3$  postperovskite is stable at up to 1,000 gigapascals and 10,000 kelvins, before dissociating into a mixture of silicon dioxide and magnesium oxide. Postperovskite should therefore be a main component of the rocky cores of Uranus and Neptune. In contrast, the rocky cores of both Jupiter and Saturn are enveloped in thick hydrogen layers, which would make pressures and temperatures too high to stabilize postperovskite.

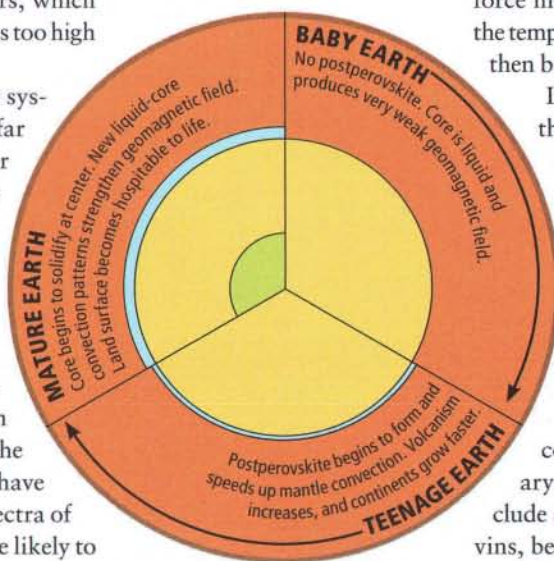
What about planets in other solar systems? All the exoplanets observed so far are bigger than Earth. Those smaller than 10 Earth masses are presumed to be Earth-like rocky planets and are called super-Earths. Astronomers have inferred the composition of exoplanets by observing their host stars. The atmosphere of our sun is similar in chemical composition to the planets of our solar system, as can be deduced from absorption lines in the sun's optical spectrum. Astronomers have similarly deduced from the optical spectra of other stars that many super-Earths are likely to have compositions similar to our own Earth's. And postperovskite may be the most abundant constituent of many of those planets, given the ranges of pressures and temperatures that would exist in their innards.

## To Be Continued

Questions remain about the structure of our planet's postperovskite-rich D'' layer. Large anomalies in seismic-wave velocities have long been observed at those depths, as if the D'' layer were not uniform but had two conspicuous fea-

## MANTLE AND CORE EVOLUTION

When the earth formed, the mantle contained no postperovskite, and the hot, iron-rich core was entirely liquid. Because the mantle was inefficient at dissipating heat, the inner earth cooled slowly (*baby earth*). Some 2.3 billion years ago, the formation of postperovskite at the bottom of the mantle speeded up convection. This change in dynamics may have increased volcanism and, with it, the growth of continents (*teenage earth*). The consequent accelerated heat transport also cooled the core enough that, around one billion years ago, a solid inner core began to form (*mature earth*). Convection patterns in the liquid-core layer became more regular and began to produce a strong geomagnetic field, which shields the earth's surface from the dangers of solar wind and cosmic rays. This may have enabled life to move onto land.



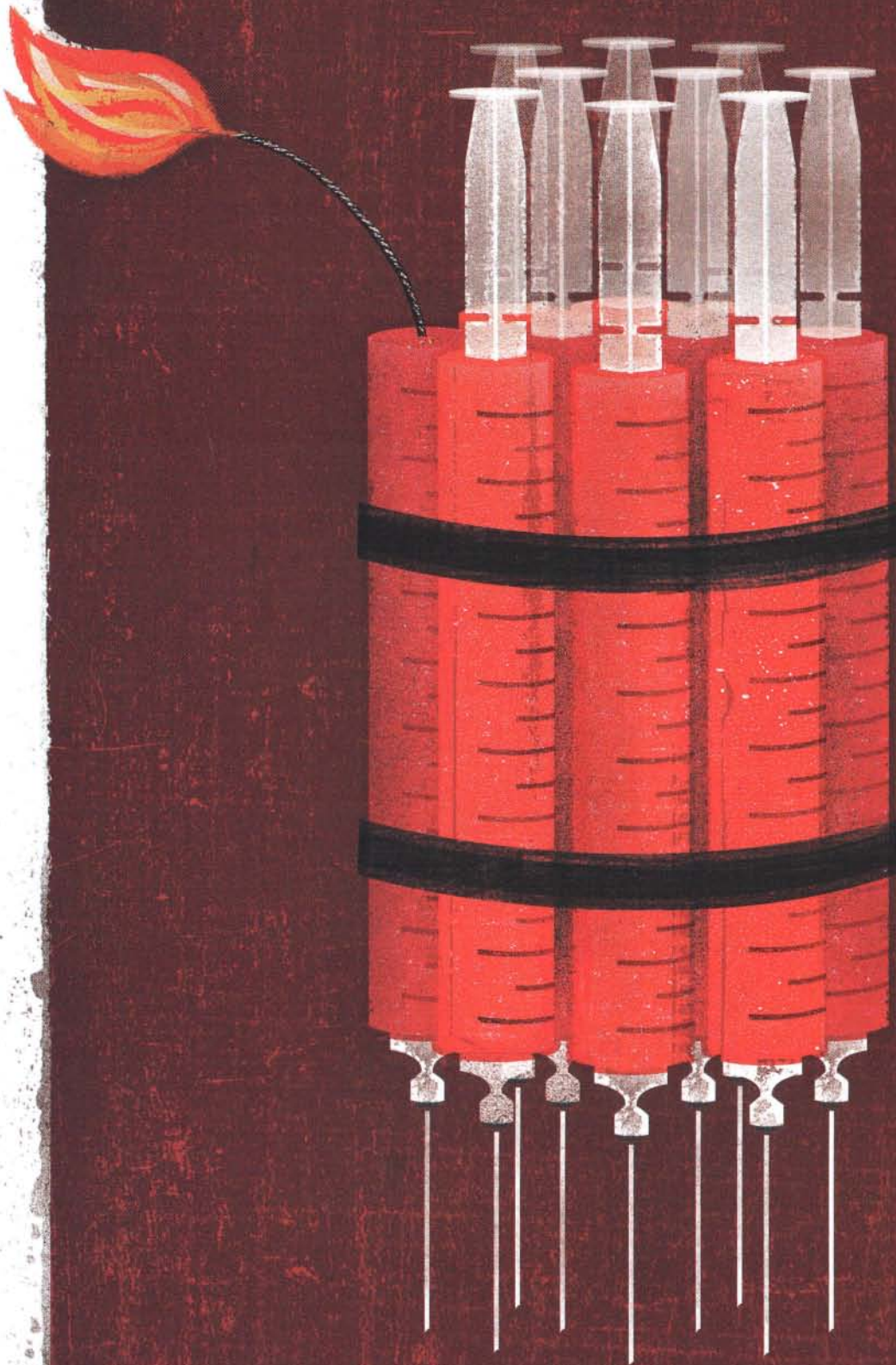
tures, one located roughly under Africa and other one under the Pacific Ocean. Could there be two masses, denser than the surrounding rock but still light enough to float on the outer core, just like the continents float on the outer mantle? These "hidden continents" could affect the flows at the bottom of the mantle and indirectly the convection patterns in the entire mantle—and thus even plate tectonics at the surface. How did these masses form, and are they growing? Could it be that the one under the Pacific Ocean had something to do with the mantle plume that produced the archipelago of Hawaii? These and other questions may be answered in the near future.

The earth's lowermost mantle has long been enigmatic, but many of its characteristics are now well explained thanks to the discovery of postperovskite. In contrast, a number of questions remain about the iron-rich metallic core. The core has been much harder to study than the mantle because until recently diamond-anvil techniques were unable to re-create the pressures and temperatures that exist in the core. Researchers could produce higher pressures by the brute-force method of shock-wave compression, but the temperatures produced by that method would then be too high.

It has been known since 1952, however, that the liquid outer core is about 10 percent less dense than pure iron or iron-nickel alloy. One or more lighter elements, such as sulfur, silicon, oxygen, carbon and hydrogen, must therefore be present, but the identification of these light elements remains highly controversial. The temperature of the core is best estimated from the melting temperature of iron alloys at a pressure corresponding to the solid-liquid boundary in the core. But the current estimates include an uncertainty of more than 2,000 kelvins, because the melting temperature depends strongly on the exact composition, which is unknown. The crystal structure of iron at inner-core conditions is also still unknown, which makes it difficult to interpret seismological observations. Very recently, however, we have produced diamond anvils that can reach the full range of pressures and temperatures that exist in the earth's core, opening the door to addressing these unsolved mysteries about the deepest part of our planet.

It will be a bit like traveling all the way to the center of the earth, if only in our imagination. ■







# FAKE BOTOX, REAL THREAT

A booming market for a counterfeit beauty product could put a deadly biological weapons agent in the wrong hands

By Ken Coleman and Raymond A. Zilinskas

**I**n early 2006 a self-styled “naturopathic” doctor, Chad Livdahl, pleaded guilty in Arizona to mail fraud and conspiracy to engage in mail and wire fraud, to misbrand a drug and to defraud the U.S. He was sentenced to nine years in prison. His wife and business partner in Toxin Research International, Inc., in Tucson, Zarah Karim, pleaded guilty to the same charges and received a six-year sentence. Both also paid heavy fines and restitution because, according to prosecutors, the couple had made at least \$1.5 million in just more than a year by peddling tiny vials of fake Botox to doctors across the U.S.

Botox, which is injected in minute amounts to smooth frown lines or relax muscle spasms, is far from the only medical product that inspires illicit manufacture and trade. The world market in counterfeit pharmaceuticals is estimated to be worth some \$75 billion annually. But the active ingredient in Botox and related products differs from the constituents of other pharmaceuticals in a profound way: in its pure form, it is the deadliest substance known to science. In fact, botulinum neurotoxin (BoNT) is grouped with the world’s most lethal potential biological weapons agents, sharing “Select Agent” status

with the pathogens that cause smallpox, anthrax and plague. This biowarfare potential puts the existence of illicit laboratories churning out the toxin and of shady distributors selling it worldwide through the Internet into a more disturbing light than most pharmaceutical fraud.

As security analysts, we undertook two years ago to explore the size and nature of this illicit global trade and have come away gravely concerned that a deadly, but once relatively inaccessible, weapons agent is now becoming as easy to get or to make as a roadside bomb. We also believe concrete steps that are inexpensive and without risk could begin to reduce this threat and should be taken as soon as possible.

## A Multitiered Market

Since 1989, when the U.S. Food and Drug Administration licensed Allergan in Irvine, Calif., to sell Botox for medical uses, the company has garnered the major share of the legitimate market for botulinum toxin products, worth some \$2 billion in sales in 2009. Other manufacturers of licensed BoNT products, particularly Ipsen, based in France, Merz Pharma in Germany and Lanzhou Institute of Biological

## KEY CONCEPTS

- Consumer demand for counterfeit products containing botulinum neurotoxin may be fueling a proliferation of illicit toxin producers.
- Botulinum toxin is a lethal poison and a potential biological weapons agent.
- Illegal manufacturers could sell toxin to terrorists or could be subversives themselves.
- Scientists and law-enforcement agents could team up to start assessing the scope of the problem as a prelude to cracking down on the counterfeiters.

—The Editors



Products in China, are making inroads, however, and in some countries outselling Allergan. The FDA approved cosmetic applications of BoNT in 2002, and today a total of only seven companies in the world have licenses to produce pharmaceutical-grade botulinum toxin for use in people. Many other companies, three of them in the U.S., supply laboratories with so-called reagent-grade BoNT, which is not approved for human use but rather for industrial and scientific applications, such as vaccine research.

Counterfeit products are sometimes mislabeled to resemble an authentic pharmaceutical brand or more often are given a sound-alike name, such as "Butox" or "Beauteous." Some are fakes in every sense, lacking any detectable BoNT, but one study published last year by Ipsen investigators Andy Pickett and Martin Mewies found that about 80 percent of the illicit BoNT products they tested did contain some of the toxin, albeit in widely varying amounts. The primary customers for these bootleg BoNT products, which typically sell for less than the legitimate versions, are unscrupulous doctors and cosmetologists who buy from illicit producers or middlemen, often via the Internet, hoping to pocket the price difference. Makers of genuine BoNT products estimate that this counterfeit market costs them hundreds of millions of dollars a year in lost sales.

The cost to people who receive counterfeit products is potentially much higher, as a 2004 incident in Florida illustrates. Vials of counterfeit cosmetic BoNT landed four people in the hospital for months, near death with severe botulism and in need of mechanical ventilation. A doctor with a suspended license had purchased the BoNT from a licensed reagent-grade producer, then injected three patients and himself with a massive overdose of toxin. Exactly how much toxin each person received is unclear, but the doctor had made the grave mistake of confusing units (one unit is equivalent to 4.8 nanograms of BoNT, or 4.8 billionths of a gram) with micrograms ( $\mu\text{g}$ ), or millionths of a gram.

Other cases of reagent-grade material illegally resold for human use have also been documented, and some evidence suggests that legitimate pharmaceutical-grade product has on rare occasion been stolen or diverted to the black market. The great majority of counterfeit products, however, have mysterious origins, mainly in Asia, and are offered by illicit sellers who may or may not also be making their own ingredients.

## IT IS ONLY A SMALL STEP FROM SELLING COUNTERFEIT PRODUCTS TO SELLING THE TOXIN ITSELF IN BULK.

### A POTENT POISON

Botulinum neurotoxin (BoNT), the main constituent in Botox and related drugs, is the deadliest substance in the world. A single molecule of toxin can paralyze one nerve cell. Just one billionth of a gram can kill a mouse.

#### LETHAL TO A MOUSE

1.2 ng

#### LETHAL TO A 70-KG PERSON:

0.09–0.15  $\mu\text{g}$   
(injected)

0.70–0.90  $\mu\text{g}$   
(inhaled)

70  $\mu\text{g}$   
(ingested)

Relative weights shown

#### 1 GRAM COULD BE LETHAL TO:

- 14,285 people (ingested)
- 1.25 million people (inhaled)
- 8.3 million (injected)

#### KEY

Nanogram (ng) = 1 billionth of a gram  
Microgram ( $\mu\text{g}$ ) = 1 millionth of a gram  
Milligram (mg) = 1 thousandth of a gram

In China alone we found 20 entities—they represent themselves as companies—that claim on their Web sites to be "certified" suppliers of BoNT and to offer cosmetic products for sale. The addresses provided on the sites often proved to be nonexistent locations or small offices that appeared to be empty fronts. Whatever the real nature of the entities behind these Web sites, they have access to genuine botulinum toxin, as the Ipsen analyses demonstrated.

Evidence suggests that the manufacture of counterfeit BoNT products has also spread to the former Soviet Union and that criminal gangs may be involved. Counterfeit pharmaceuticals have been a common problem in Russia for some time, so we were not surprised to learn from experts there that an estimated 90 percent of Russian cosmetology clinics are using counterfeit BoNT products at least some of the time. One security consultant described a purveyor of counterfeit BoNT products that has been operating in Russia for more than three years. The source of these products is reportedly located somewhere in Chechnya, and its representative flies regularly to St. Petersburg carrying suitcases filled with vials bearing labels almost identical to legitimate Botox packaging. When one client asked how much product could be purchased, the representative is alleged to have replied that any quantity, even 1,000 vials, could be supplied.

We believe there is a danger that India's counterfeit drug producers, if not already involved in the illicit BoNT business, soon will be as well. The country has a legitimate producer of a BoNT product called BOTOGenie, launched in 2007, and a vibrant domestic market for both cosmetic and therapeutic BoNT products. The Indian medical tourism industry catering to foreigners seeking inexpensive care is also expanding rapidly, which is likely to entice the country's well-documented pharmaceutical counterfeiting rings to cash in.

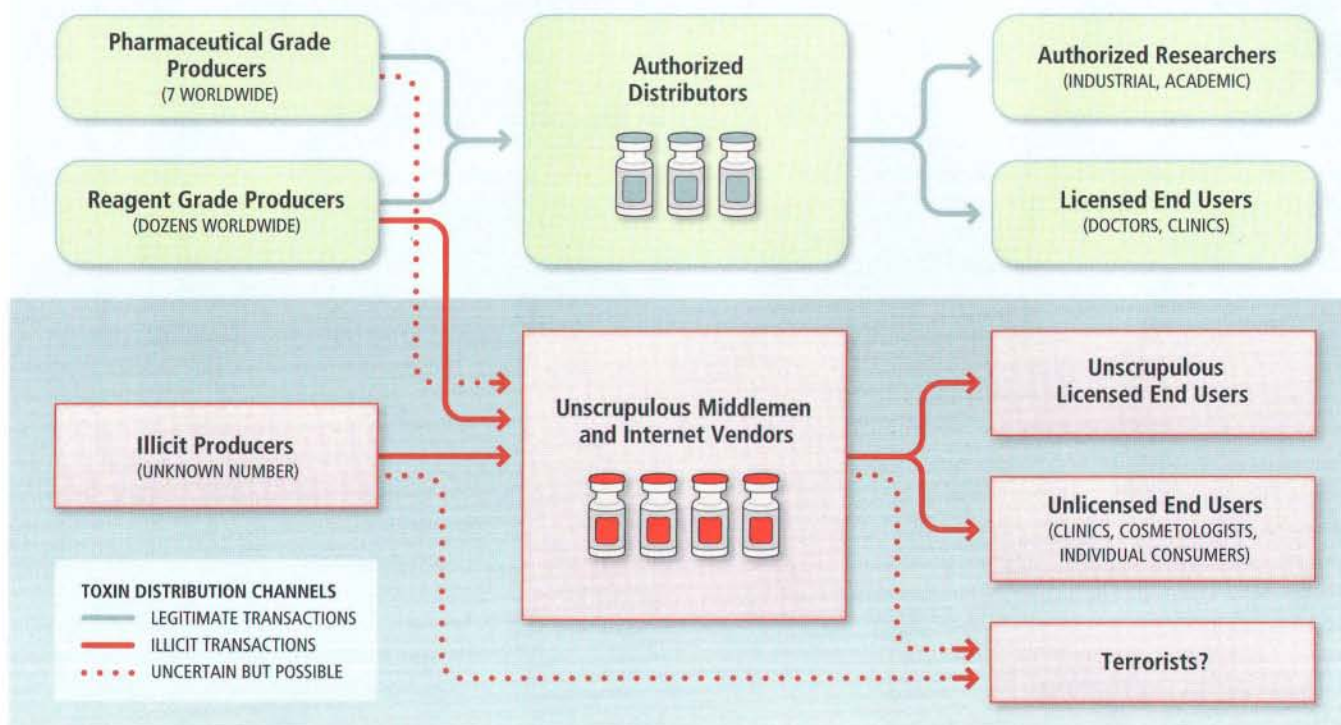
From a security perspective, this booming market is troubling because, for manufacturer-distributors it is only a small step from selling counterfeit BoNT products for cosmetic uses to selling the botulinum toxin itself in bulk quantities directly to subversive interests. Indeed, as the Russian example illustrates, such distinctions may already be blurred. And there is little to stop counterfeiters or criminals from setting up a manufacturing facility, because making botulinum toxin requires no exotic equipment and only moderate expertise in microbiology.



## [THE PROBLEM]

# Open Market for a Lethal Weapon

Avid consumer demand for cosmetic products containing botulinum neurotoxin is fueling the growth of an illicit global market for counterfeit versions. The number of illegal producers making toxin to meet that demand is unknown but is very likely growing as well. Those shady manufacturers, unscrupulous local middlemen and anonymous Internet vendors willing to ship worldwide are all potential sources from which terrorists could procure significant amounts of the toxin.



## Easy to Make, Harder to Deploy

*Clostridium botulinum*, the bacterium that produces BoNT, exists naturally in soil, but it is anaerobic, meaning that it thrives only in oxygen-free conditions. In the past, the most common source of botulinum toxin poisoning—botulism—in the U.S. was food, such as damaged or unsterilized canned goods. The more common form in adults today is wound botulism, which occurs mostly among addicts who infect themselves with *C. botulinum* while injecting drugs.

The pure toxin that the microbes generate is, on its own, the most potent poison in the world. And manufacturing the minuscule amounts of it that are required to kill takes only equipment standard in biology laboratories worldwide. In less than a month, someone with the equivalent of a master's degree in biology could probably accomplish the necessary steps to produce enough toxin to cause mass casualties.

BoNT is so potent that a single molecule of toxin is believed to be capable of incapacitating one nerve cell. The toxin particles block receptors on nerve endings, silencing the nerves and

## [THE AUTHORS]



**Ken Coleman and Raymond A. Zilinskas** collaborate at the James Martin Center for Nonproliferation Studies of the Monterey Institute of International Studies in California. Coleman, a former microbiologist, is a senior fellow at the institute and a medical technology entrepreneur. Zilinskas, also a former microbiologist, directs the center's chemical and biological weapons nonproliferation program. He has been a longtime consultant to the U.S. government and was a United Nations inspector in Iraq in 1994.

paralyzing surrounding muscles. When pure BoNT is injected into a vein or muscle, just 0.09 to 0.15 µg can kill a 70-kilogram person. Although inhalation delivers the toxin to nerve fibers less efficiently, a mere 0.70 to 0.90 µg of inhaled toxin can be deadly to an adult. Ingesting BoNT is actually the least effective method of poisoning oneself, requiring 70 µg. Put another way, one gram of BoNT potentially contains more than 14,000 lethal doses delivered orally or about 1.25 million lethal doses if inhaled.

All *C. botulinum* strains found in nature are capable of producing BoNT, although the strains used by legitimate manufacturers are naturally occurring hyperproducers of toxin. One in particular, known as the Hall strain, is also widely employed in academic labs and stored in national cell culture collections. A would-be toxin manufacturer with access to the bacterium would have no problem finding out how to use it because instructions have been widely published in the scientific literature over the past 50 years.

The process begins with a small colony of



*C. botulinum*, suspended in a common nutrient broth and allowed to multiply in incubators and fermenters for a total of three to four days. This mixture is then removed from the fermenter and centrifuged or filtered to separate out the liquid containing concentrated toxin. Of course, the pharmaceutical industry performs additional purification steps to ensure the quality and stability of their final product, which is sold as a fine powder packaged in a small vial. When the end user is ready to reconstitute the material, adding 10 milliliters of saline to the vial dissolves the powder in seconds. This liquid formulation must then be used within a few hours, because it quickly loses potency.

The relative fragility of the toxin once it is exposed to the environment has been a substantial obstacle in past efforts to weaponize BoNT. The U.S. and U.S.S.R. nonetheless succeeded in developing weapons that dispersed BoNT as an aerosol. Iraq developed BoNT-containing bombs, which would probably have been next to useless. The only well-documented attempt by a nonstate actor to deploy botulinum toxin as a weapon occurred in the early 1990s. The apocalyptic Japanese cult Aum Shinrikyo, whose membership included medical doctors and a scientist, attempted several times to disperse aerosolized BoNT through sprayers hidden in briefcases. These attacks failed, but only because the strain of *C. botulinum* the group's scientist used was a poor toxin producer, sprayer nozzles got clogged and some guilt-ridden operatives failed to activate their devices.

The most plausible scenarios for terrorist use

## THE UNIQUE ROLE OF THE INTERNET IN FACILITATING SUPPLY AND DRIVING DEMAND MAKES THE THREAT MORE IMMEDIATE.

of BoNT involve sabotage of food or beverages. One study published in the *Proceedings of the National Academy of Sciences USA* in 2005 analyzed possible strategies for introducing the toxin at key points in the cow-to-consumer milk supply chain. The paper provoked controversy for identifying a sabotage method that might succeed. Yet its authors, Lawrence M. Wein and Yifan Liu of Stanford University, could not have known five years ago that terrorists attempting this kind of attack today would be able to purchase the toxin needed for their plan from an anonymous Internet source instead of having to manufacture it themselves. Their hypothetical plot now seems that much easier to carry out.

### Assessing the Threat

Attempts by the international security community to prevent the proliferation of biological and chemical weapons usually focus on limiting demand by pressuring countries not to engage in weapons development and constraining supply by tightly controlling traffic in weapons-making equipment and know-how. Export controls and treaties, such as the 1972 Biological and Toxin Weapons Convention and the 1993 Chemical Weapons Convention, were developed by governments for governments, however. The international proliferation of illicit botulinum toxin products creates an entirely new and perplexing situation because the toxin-making supplies are not sought by governments but by individuals and because demand for the toxin is not driven by governments but by consumers.

The unique and important role of the Internet

### [STRATEGY]

## Gauging the Scale of the Problem

To begin combating illegal BoNT production, law-enforcement agents could team with scientists to assess how many manufacturers are operating. Posing as clinic operators, agents could order BoNT products from a range of online sellers **1**. Laboratory analysis could then discern a unique "product signature" characteristic of each producer **2**. The signatures would indicate how many producers exist and offer clues to their locations and the sources of raw materials they used to make the toxin **3**.



#### 1 ORDER BoNT PRODUCTS ONLINE



LAW-ENFORCEMENT FRONTS



PRODUCT SAMPLES

#### 2 PERFORM PRODUCT-SIGNATURE ANALYSIS ...



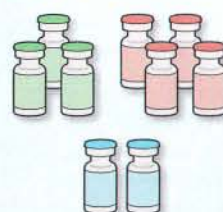
**EXAMINE:**  
DNA—traces of bacterial DNA



**CHEMISTRY**—metals and other trace elements in water and other chemicals used in drug formulation



**ENVIRONMENTAL CONTAMINANTS**—pollen and other spores



UNIQUE PRODUCER SIGNATURES

#### 3 ... WHICH REVEALS:

- Number of producers operating
- Identity of bacterial strains used to make toxin
- Clues to geographic origin, from water and environmental residues
- Possible suppliers of chemical raw materials



in both facilitating supply and in driving demand also makes the proliferation of the botulinum toxin threat more immediate than is the case for any other potential biological or chemical weapon. Our study documented a substantial increase in Internet vendors in the past two years, yet the possibility that these sellers represent a comparable proliferation in illicit BoNT manufacturers has not yet garnered much attention from agencies charged with preventing bioterrorism or suppressing the counterfeit pharmaceutical trade. Instead it is falling into the cracks between the two jurisdictions.

Indeed, some traditional weapons-interdiction strategies are likely to be ineffective against this novel threat. Attempting to affect the supply side of this equation by limiting equipment or information, for example, cannot seriously deter would-be BoNT manufacturers because the commonplace materials needed to make the toxin and the bacterium itself are too widespread.

Limiting demand for counterfeits might help discourage illicit manufacturers. Producers of pharmaceutical-grade toxin are employing advanced labeling technologies, such as holograms and verifiable serial numbers on packages so that doctors and cosmetologists can be assured they have genuine products. To educate end users about the dangers of counterfeits, Ipsen researchers have also made parts of their analyses of counterfeit products available to the public in lectures, poster sessions and scientific articles.

Allergan has taken quiet and selective steps toward stemming counterfeiting, including collaborating with investigators in China to close down one illicit BoNT operation in Shanxi Province. Because the number of illegal BoNT laboratories is large and likely to increase, however, companies have neither the expertise, the resources nor the authority needed to track down and prosecute these criminals.

A different example of pharmaceutical counterfeiting may offer a more effective approach. Only a few years ago the antimalaria drug artesunate had become the object of a robust counterfeit market. By 2007 one third to one half of all artesunate sold in Southeast Asia was actually counterfeit product, most of it therapeutically useless. As a result, licensed artesunate manufacturers were not only losing money, malaria victims were dying and the disease was spreading because so many patients were going untreated. That same year, a relatively complex international cooperative effort code-named



## COUNTERING COUNTERFEITS

Holograms incorporated in the label of an authentic Botox vial are difficult to replicate and assure end users that the container is legitimate. Licensed BoNT-product makers may also employ other packaging details to enhance security and educational efforts to warn the public, but they lack the resources and the authority to pursue counterfeiters.

## MORE TO EXPLORE

**Botulinum Toxin as a Biological Weapon: Medical and Public Health Management.** Stephen S. Aron et al. in *Journal of the American Medical Association*, Vol. 285, No. 8, pages 1059–1070; February 28, 2001.

**Beauty and the Beast.** Donald Kennedy in *Science*, Vol. 295, page 1601; March 1, 2002.

**Encyclopedia of Bioterrorism Defense.** Edited by Richard F. Pilch and Raymond A. Zilinskas. Wiley, 2005.

**Serious Issues Relating to the Clinical Use of Unlicensed Botulinum Toxin Products.** Andy Pickett and Martin Mewies in *Journal of the American Academy of Dermatology*, Vol. 61, No. 1, pages 149–150; July 2009.

Additional supporting material:  
[www.fakebotoxrealthreat.com](http://www.fakebotoxrealthreat.com)

Operation Jupiter was mounted for the specific purpose of suppressing this counterfeit artesunate trade. Collaborators in the offensive included representatives from the Wellcome Trust, Interpol, the Royal Canadian Mounted Police, the Australian Therapeutic Goods Administration, the Intellectual Property Division of the Chinese Ministry of Public Security, the World Health Organization, the U.S. Centers for Disease Control and Prevention, and several other smaller agencies and nongovernmental organizations.

Although Operation Jupiter holds many lessons for attempts to suppress counterfeit drugs, one of the project's most notable and important activities was the collection of hundreds of samples of counterfeit artesunate sold at five different sites in Cambodia, Laos, Myanmar (Burma), Thailand and Vietnam. These samples were transported to high-quality reference laboratories and subjected to detailed analyses that constructed a "product signature" for each sample. These unique profiles allowed analysts to deduce how many different illicit artesunate producers were operating, and with that information in hand, law-enforcement agents could begin matching the products sold by intermediaries to the original manufacturers and sketching the outlines of distribution networks. In this way, at least some of the counterfeit products were traced to southeast China, enabling officials there to break up that criminal operation.

We do not delude ourselves about how difficult it would be to convince governments to partake in such an effort against counterfeit botulinum toxin producers. We do believe the Operation Jupiter example is relevant because it offers a scientific approach to at least beginning to understand the scope of the problem. If law-enforcement agencies took just the first step of setting up phony clinics to buy illicit BoNT products, then laboratory analyses could begin to establish how many illegal producers are operating. The data could later be used to pursue the criminals or could point to possible toxin sources in the event of an attack.

As security analysts, we know there are myriad theoretical threats to public safety. Only very few biological and chemical agents can be used by nonstate actors to cause mass casualties, however, and now none is as easy to procure as BoNT, because of illicit manufacturing and Internet trade. Vanity is currently driving the highly profitable market for counterfeit BoNT products, but it would be folly to assume that subversives have not noticed that booming business, too. ■



## Industrious Ants ■ Seeds of Despair ■ Discovering Antarctica

BY KATE WONG

### → ADVENTURES AMONG ANTS: A GLOBAL SAFARI WITH A CAST OF TRILLIONS

by Mark W. Moffett. University  
of California Press, 2010 (\$29.95)



Join biologist and photographer Mark W. Moffett of the Smithsonian Institution—who has been called the “Indiana Jones of entomology”—as he journeys to the Amazon, Nigeria, Borneo and beyond to uncover the secret lives of ants.



### EXCERPT

#### → PANDORA'S SEED: THE UNFORESEEN COST OF CIVILIZATION

by Spencer Wells. Random House, 2010 (\$26)

*Around 10,000 years ago humans invented agriculture, shedding the hunter-gatherer lifestyle for one in which they created their own food. This innovation, argues anthropologist and geneticist Spencer Wells, set into motion a chain of events that would ultimately lead to our present era of overpopulation, infectious disease and anxiety—a mismatch between culture and biology. Below he describes modern-day stresses and their impact on our still fundamentally hunter-gatherer minds.*



“Cars rush by outside your window, a horn blaring occasionally. The refrigerator hums in the corner of the kitchen, and the heat coming out of a duct over your head whooshes softly. Bills sit stacked on the counter, insistently waiting to be opened. A television—perhaps one of several in the house—blares advertisements from the next room, and Internet pop-up ads interrupt your attempts to check on your retirement investments. The cacophony reaches a crescendo when your spouse’s cell phone rings, vibrating along the tabletop like some sort of angry digital dervish. The blare of the outside world goes on all around us, even while we attempt to focus on our ‘real’ lives.

“We are constantly surrounded by surreptitious stimuli—so much so that we take it all for granted. We are used to the notion that advertisements saturate our lives—exposure estimates for the average American range from several hundred to several thousand every day—as promoters try to sell us everything from life insurance to an enhanced sex life. Data flows at us from every direction. Information is ubiquitous and, with the rise of the Internet and broadband connectivity, more easily accessible than ever. But even things we might not think of as intrusive bombard our subconsciousnesses with stimuli. Inadvertently, the machines we have created to improve our lives may actually be causing some degree of psychological harm....

“Our lives are now lived in a state that could be called ‘stream of subconsciousness,’ as we subliminally lurch from one unrelated (and usually unwanted) stimulus to the next like floating dust particles buffeted by the random forces of air currents. Some people seem to thrive on constant overstimulation ... but most of us react rather badly to it.”

### ALSO NOTABLE

#### BOOKS

- **How Pleasure Works: The New Science of Why We Like What We Like**  
by Paul Bloom. W. W. Norton, 2010 (\$26.95)
- **The Matchbox That Ate a Forty-Ton Truck: What Everyday Things Tell Us about the Universe**  
by Marcus Chown. Faber and Faber, 2010 (\$25)
- **The Evolution of Childhood: Relationships, Emotion, Mind**  
by Melvin Konner. Belknap Press, 2010 (\$39.95)
- **Bonobo Handshake: A Memoir of Love and Adventure in the Congo**  
by Vanessa Woods. Gotham, 2010 (\$26)
- **The Rational Optimist: How Prosperity Evolves**  
by Matt Ridley. Harper, 2010 (\$26.99)
- **Unhinged: The Trouble with Psychiatry**  
by Daniel Carlat. Free Press, 2010 (\$25)
- **Barnum Brown: The Man Who Discovered *Tyrannosaurus rex***  
by Lowell Dingus and Mark Norell. University of California Press, 2010 (\$29.95)
- **The Eerie Silence: Renewing Our Search for Alien Intelligence**  
by Paul Davies. Houghton Mifflin Harcourt, 2010 (\$27)
- **The Pythagorean Theorem: The Story of Its Power and Beauty**  
by Alfred S. Posamentier. Prometheus Books, 2010 (\$33.50)
- **The Secret Life of the Grown-up Brain: The Surprising Talents of the Middle-Aged Mind**  
by Barbara Strauch. Viking, 2010 (\$26.95)



#### EXHIBITS

- **The Race to the End of the Earth**  
May 2010–January 2011 at the American Museum of Natural History in New York.

#### 1912 SOUTH POLE EXPEDITION



- **The Deep** May 28–September 5 at the Natural History Museum in London.



# Presidential Harrismen

Poll results you don't want to touch with a 10-foot poll

BY STEVE MIRSKY



In early March, Harris Interactive conducted an online survey to gauge the attitudes of Americans toward President Barack Obama. The Harris Poll generated some fascinating data. For example, 40 percent of those polled believe Obama is a socialist. (He's not—ask any socialist.) Thirty-two percent believe he is a Muslim. (I had predicted that a Mormon, Jew, Wiccan, atheist and Quetzalcoatl worshipper would become president before America elected a Muslim, so a third of this country actually may be quite open-minded, in an obtuse way.) Also, 14 percent believe that Obama may be the Antichrist. Of those who identified themselves as Republicans, 24 percent think Obama might be.

Scientific polling may include multiple questions designed to measure the internal consistency of the responses of those being surveyed. To measure the consistency of the responses of those who think Obama might be the Antichrist, we have prepared an extension of the poll.

Please answer the following questions “yes” or “no”:

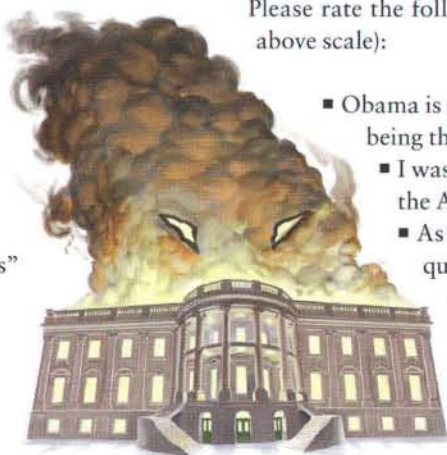
- Do you consider your belief that Obama only *might* be the Antichrist to be a sign of your open-mindedness and scientific outlook?
- Have you ever called a local TV news office because you saw an image of a major religious figure in (a) a piece of toast, (b) tree bark or (c) a Sheetrock water stain?
- Were you surprised that the president might be the Antichrist because, according to the movie *The Omen III*, the U.S. ambassador to England should be the Antichrist?
- Do you think Earth is only 6,000 years old?
- Have you had the fillings of your teeth removed to rid your person of the tracking devices placed by the government?

This poll also found that 22 percent of Republicans think that Obama “wants the terrorists to win.” We assume most of those 22 percent who think that Obama “wants the terrorists to win” are among the 24 percent who think that Obama may be the Antichrist. Therefore, a small percentage of Republicans who think that Obama may be the Antichrist also think that Obama wants the terrorists to lose. If that group includes you, please rate the

following three statements from 1 to 5 (1 is “strongly disagree,” and 5 is “strongly agree”):

- The Antichrist wants us to beat the terrorists so he can take credit for it, thereby making it easier for him to accomplish his ultimate nefarious goal.
- The Antichrist considers himself to be in competition with the terrorists because they do not recognize his authority on matters of all things evil.
- The Antichrist *would* root *against* terrorists because it is just like him to be tricky like that.

Please rate the following 10 statements from 1 to 5 (using above scale):

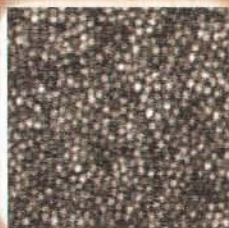


- Obama is not the first person I have suspected of being the Antichrist.
- I was pretty sure that Bill Clinton was the Antichrist.
- As Pat Robertson noted, the Haiti earthquake was the direct result of Haitians making a pact with Satan more than 200 years ago.
- Pat Robertson is wrong about the Haiti earthquake, because earthquakes are caused by living people behaving immorally.
- Hurricanes are also caused by people behaving immorally.
- Volcanic eruptions are also caused by people behaving immorally.
- But climate change is a hoax.
- I saw Sarah Good with the Devil!
- I saw Goody Osburn with the Devil!
- I saw Bridget Bishop with the Devil!

Thank you for participating in this poll. Some respondents may feel this survey is another example of leftist political bias. In fact, these questions and statements are designed not to find out whether an individual has a specific political viewpoint but rather to determine whether the respondent is a minor, middling or major crank. The results are crucial for the proper stocking of personnel and resources of the FEMA internment camps. Again, thank you—and don't forget to mail in your census form. ■



# Advanced adaptive optics help create a sharper, truer view of the inside of your eye...



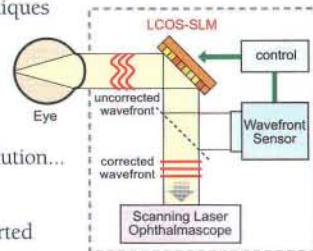
## Reduced distortion, higher resolution

For years, researchers have examined the fundus or inner lining of the eye by looking through the pupil with an ophthalmoscope. However, the eye's cornea and lens have always *distorted* their view.

And early techniques for correcting the distortion were too costly and low in resolution...

So in 2005, Hamamatsu started working on a better solution. The answer

was Liquid Crystal on Silicon Spatial Light Modulator technology (LCOS-SLM). It applies controlled low voltages across a special liquid crystal-mirror



Adaptive Optics Scanning Laser Ophthalmoscope using LCOS-SLM

## Hamamatsu is opening the new frontiers of Light \* \* \*

to dynamically alter the refractive index at each pixel and precisely correct wavefront distortions.

In the future, this technology may enable new



Get focusable views of visual receptor cells, blood vessels and nerve fibers (left to right).

generations of lower-cost, high-resolution fundus

imaging. Such as scanning laser ophthalmoscopes that can clearly focus on individual visual receptor cells and microscopic blood vessels.

Or the technology may help to make earlier diagnosis of eye and circulatory system diseases. It's just one more way Hamamatsu is opening the new frontiers of light — to brighten our world.

<http://jp.hamamatsu.com/en/rd/publication/>

**HAMAMATSU**

Photon is Our Business

Hamamatsu's work on this technology was conducted under a research project of the New Energy and Industrial Technology Development Organization of Japan (NEDO). The adaptive optics scanning laser ophthalmoscope is being developed and reviewed with cooperation from NIDEK Co., Ltd. and the Faculty of Medicine at Kyoto University under this project.